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ELECTIVE PLASTIC REPAIR OF CONGENITAL DEFECTS

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IT is not surprising that the parents of an infant recently born with a congenital anomaly are interested primarily in how soon the defect can be repaired. It would be ideal if all such procedures could be carried out immediately after birth. Of course, if immediate repair is essential to survival, it matters little whether or not the immediately postnatal period is the time of election for operation. Most congenital anomalies, particularly those managed by the plastic surgeon, tolerate postponement until the optimum time for surgical repair. This particular moment varies considerably, not only from patient to patient, but from surgeon to surgeon. For example, one surgeon may elect to repair a cleft lip as soon as possible after delivery, while another defers treatment for six or more weeks. Various factors such as inadequacy of available anesthesia, unsatisfactory operating room facilities, or inadequate nursery care may also influence this decision.

From the practical standpoint, it is possible to set up several criteria that are useful in determining the ideal times for these procedures. First, the mortality associated with the elective operation must be small, and the time selected for the procedure should not modify this figure. Second, subsequent function and normal growth should be interfered with as little as possible. Finally, the feelings of the infant's parents cannot be ignored. It frequently is cruel if not impossible to keep emotionally distraught parents waiting weeks or years for the arrival of the ideal date.

The plastic surgeon is called upon to repair a number of these congenital anomalies, specifically those in which subsequent cosmetic appearance is a

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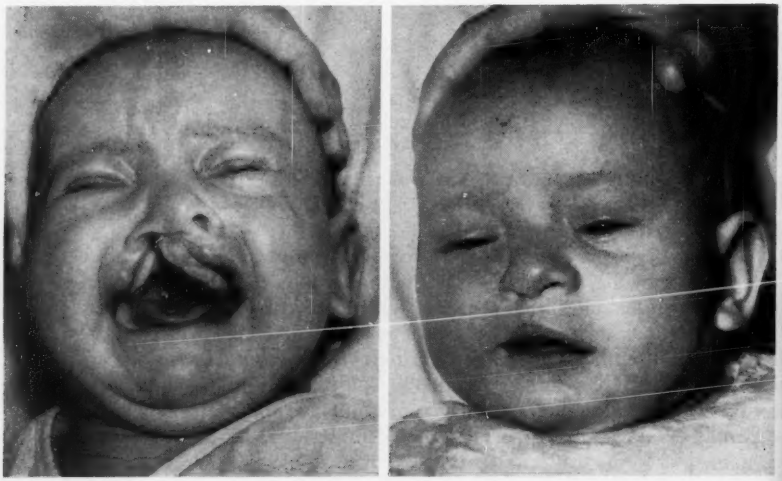
factor, and those for the repair of which various plastic technics are required. The most common defects are cleft lip, cleft palate, deformities of the external ear, webbed fingers, hypospadias, congenital ptosis of the eyelid, and anomalies of branchial cleft origin. The purpose of this paper is to present a brief discussion of procedures of choice and a reasonable timetable for their surgical repair.

Cleft Lip and Palate

Cleft lip, cleft palate, or the combined defect is found once in approximately 800 newborn infants. Surgical procedures for their primary repair have become reasonably well standardized and the probability of good cosmetic and functional results is high (Fig. 1).



(A) (B)

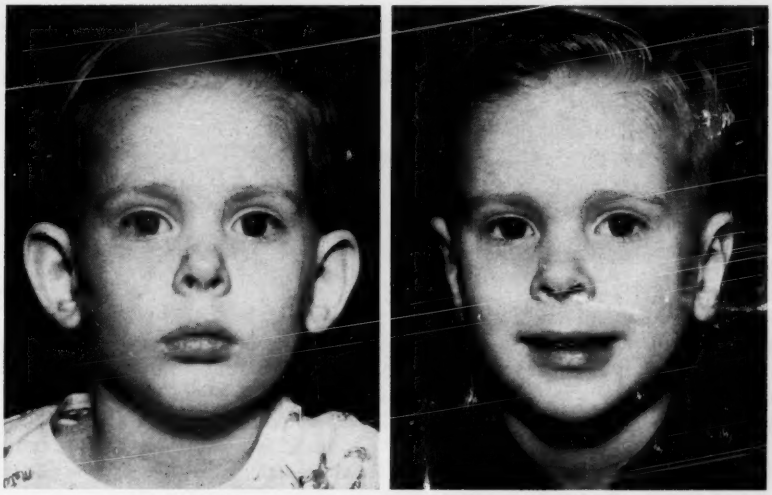
Fig. 1. (**A**) Preoperative photograph of a three-month-old infant with wide unilateral cleft lip. (**B**) Photograph showing results after repair by the triangular flap method.

For the unilateral cleft lip, most plastic surgeons employ a flap repair using either a triangular or a square flap just above the lip vermilion, to overcome the problems inherent in linear approximation of the lip margins.[1] Repair of the double lip requires similar closures on each side, usually carried out in one operation. The time of choice for this repair is the immediately postnatal period. The earlier that surgery is completed, the less the emotional trauma that is inflicted on anguished parents. Moreover, the infant tolerates the procedure well, whether it be carried out on the day of birth or within the first few weeks thereafter. After postoperative hospitalization of nine or 10 days, the essentially normal-appearing infant is returned to his mother only a few days after her own discharge from the hospital.

There has been and continues to be sporadic argument as to the advisability of early repair of the cleft palate. Some surgeons recommend postponement of repair until the child is five or more years old, on the ground that facial bone development is interfered with by early repair. The evidence for this interference is inconclusive, and the majority of plastic surgeons recommend surgical repair when the child is between 14 and 18 months of age.[2] This period of time allows considerable growth both of the oral cavity and of the palatal flaps, and at the same time assures closure of the palate before improper speech habits have become established. The Von Langenbach operation, with its lateral relaxing incisions and thorough undermining of the palate flaps, is employed. Set-back operations designed to lengthen the short palate may be used at the time of primary closure, but usually are deferred until such time as a real need for such lengthening is demonstrated.

Deformities of the External Ear

The so-called "lop-ear" deformity, or prominent ears, is associated either with an insufficiently sharp, or an absent ante-helix. Its proper repair requires complete breaking of the cartilage spring, with removal of a strip of cartilage, if necessary, to make an ante-helix stand out from the head at normal height (Fig. 2). The primary consideration as to time of operation is that it be prior to school



(A) (B)

Fig. 2. (**A**) Preoperative photograph of a four-year-old child with bilaterally prominent ears (**B**) Photograph showing results after surgical repair.

age, to avoid the emotional complications incident to the inevitable teasing of young children at that time. Since a little co-operation on the child's part makes infinitely more pleasant the application of dressings, removal of sutures, and subsequent protection of the newly repaired ears, the operation usually is scheduled during the summer of his fourth or fifth year.

Congenital absence of all or part of an ear also is repaired at about this time, allowing approximately a full year for its completion.[3] The actual procedure consists of initial utilization of existing ear remnants to fit into the proposed reconstruction; implantation of shaped, preserved, or autogenous cartilage; and finally, elevation of the ear flap with the included cartilage and resurfacing of its medial surface and adjacent scalp with a skin graft. Absence of the associated external ear canal is repaired only if a bony canal and associated middle-ear structures can be roentgenographically demonstrated. Normal function of such a reconstructed canal also requires the presence of an ear drum.

Webbed Fingers

The separation of webbed fingers and skin grafting of their raw surfaces is deferred until the immediately preschool age, provided that growth of the individual digits is proceeding normally and that there is no evidence of interference with function of any of the fused parts. The reasons for this choice of time are the larger size of the fingers, the increase in understanding of the older child and in his ability to co-operate. More fundamental deficiencies requiring bone and tendon repair or digit reconstruction may be taken care of at this age, but usually are deferred until considerably later because of the great need for patient education and co-operation (Fig. 3).

Webbed toes offer little cosmetic problem to the patient of any age and are repaired only rarely—and then only when such repair is demanded by anxious parents.

Hypospadias

Several methods are available for the repair of hypospadias. All methods require meticulous removal of the fibrous tissue associated with the chordee. They differ only in the technic for constructing the skin-lined urethral channel on the shaft of the penis. The most common and probably most successful procedure is that in which the tube is constructed from local skin flaps.[4] Its completion requires either two or three operations during a period of from three to nine months, barring complications. Repair is deferred as long as possible to permit maximum penile growth and to obtain maximum co-operation from the patient. The requirement that a boy stand to urinate makes it necessary to proceed with the reconstruction prior to school age if the ridicule of schoolmates is to be avoided.

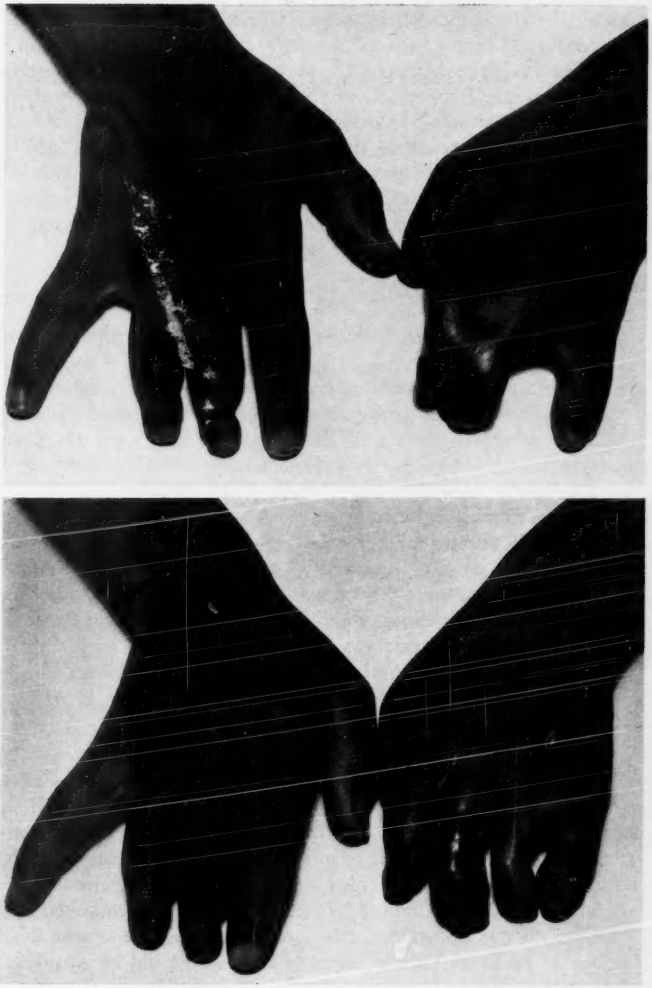


Fig. 3. (**A**) Preoperative photograph of the hands of a nine-year-old child with severe syndactylism already interfering with growth and function. (**B**) Photograph showing results after surgical repair.

Congenital Ptosis of the Upper Eyelid

Congenital drooping of the upper eyelid may be partial or complete, unilateral or bilateral. If it is minimal, with almost normal function of the levator

muscle, the Blascovicz operation, in which the muscle itself is shortened, preserves optimal function as well as produces a good cosmetic result. If the degree of ptosis is moderate or severe, the procedure of choice is the insertion of a fascia lata sling attached superiorly to the fascia covering the frontalis muscle of the forehead. This allows full mobility of the eyelid controlled by the frontalis, without undue exposure of the globe at rest. A minimal deformity may be corrected at any time in the preschool period. The more severe deformity may result in visual difficulties, with positioning of the head and neck to permit vision beneath the ptotic lid. It is essential that repair be carried out before these complications develop and cause permanent damage.

Anomalies of Branchial Cleft Origin

Most branchial cleft remnants are invisible or unnoticed at birth, becoming obvious only with the appearance of swelling or a fluid discharge through a small skin orifice on the neck. There is no particular time of choice for their elective repair; excision is advised when they are discovered, on the basis that sooner or later they will become infected and require surgical treatment under more difficult circumstances.

The small preauricular sinuses frequently occurring just anterior to the external ear often are considered as being branchial cleft remnants. There is little evidence to support this view; they more likely are sinuses associated with lines of fusion of the various embryonic segments of the ear itself. If they become infected, excision is necessary.

Other Anomalies

Brief mention should be made of several less common anomalies. Congenital facial paralysis is fortunately only partial in most instances. If sufficient facial nerve function is present to provide even slight tone to the facial musculature, operative repair can do little to improve the condition and may do considerable damage to minimally functioning structures. In the absence of any demonstrable function, mechanical support by fascia lata may be employed in the childhood period, with the knowledge that additional surgery is practically inevitable. The use of masseter muscle slings or the like should be avoided, at least until adolescence. Exploration or graft of the facial nerve is of no value.

Facial hemiatrophy is a most difficult surgical problem for which no completely satisfactory solution has been proposed. Every possible material, from skin to shredded polyethylene, has been buried as a free graft beneath the skin to provide normal facial contours with little success. It appears that the recently reported dermal-fat pedicle,[5] i.e., a graft of fat with an attached layer of dermis and carrying its own blood supply, may offer the best approach. The evidence is good that such transplanted fat and dermis will survive without serious shrinkage.

References

1. Anderson, R.: Repair of cleft lip. Cleveland Clin. Quart. **21:** 180-186, 1954.

2. Bill, A. H., Jr.; Moore, A. W., and Coe, H. E.: Time of choice for repair of cleft palate in relation to type of surgical repair and its effect on bony growth of face. Plast. & Reconstruct. Surg. **18:** 469-473, 1956.

3. Steffensen, W. H.: Comments on reconstruction of external ear. Plast. & Reconstruct. Surg. **16:** 194-200, 1955.

4. Byars, L. T.: Functional restoration of hypospadias deformities; with a report of 60 completed cases. Surg., Gynec. & Obst. **92:** 149-154, 1951.

5. Neumann, C. G.: Use of large buried pedicled flaps of dermis and fat; clinical and pathological evaluation in treatment of progressive facial hemiatrophy. Plast. & Reconstruct. Surg. **11:** 315-332, 1953.

TREATMENT OF GOITER IN CHILDREN

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1. *THE changing picture of endemic goiter.* With the increased transportation of frozen foods from one portion of the country to another, and with the widespread use of iodized salt, there are few if any areas in the United States where most people do not receive an adequate amount of iodine. For this reason, the naturally iodine-deficient areas, in which goiter formerly was endemic, no longer produce a high incidence of goiter. In the areas in which goiter once was endemic, the goiters that are seen today are sporadic and familial rather than endemic in character. Because these goiters rarely are the result of iodine deficiency, treatment with iodine is not apt to be helpful.

2. *Nontoxic diffuse goiter.* Two types of nontoxic diffuse goiter occur today in children. One may be called "hypofunctional hyperplasia" of the thyroid, and the other is struma lymphomatosa.

(a) *Hypofunctional hyperplasia.* This condition may be seen in newborn infants; it may occur in early infancy; or it may develop during childhood. It is characterized by a high uptake of radioiodine (I^{131}) usually without an increase in the amount of protein-bound iodine. The basic defect is the failure of the thyroid gland to synthesize properly functioning thyroid hormone. The thyroid may maintain its ability to concentrate iodine, but it cannot incorporate the iodine into a properly functioning hormone.[1] For this reason, hypothyroidism develops; the pituitary is stimulated to increase its output of thyrotropic hormone; the thyroid responds by hypertrophy and hyperplasia; and a diffuse goiter develops. Biopsy specimens of such goiters show diffuse hyperplasia histologically indistinguishable from that seen in Graves' disease, but clinically no evidence of hyperthyroidism is present.

The administration of iodine to a patient with hypofunctional hyperplasia increases rather than diminishes the hypothyroidism, and results in an even greater thyroid deficiency and in even more rapid hypertrophy and hyperplasia of the gland. The problem here is not a deficiency of iodine but a deficiency in the mechanism that incorporates iodine into thyroid hormone. The administration of iodine in large doses to patients with this type of gland appears to suppress further the ability of the gland to make thyroid hormone, just as it does to a much more striking degree in patients with Graves' disease. Consequently the growth of the gland is not suppressed by feeding iodine but is stimulated.

The proper treatment for hypofunctional hyperplasia is administration of desiccated thyroid. An adequate exogenous supply of hormone relieves the gland of the necessity of making thyroid hormone, suppresses the output of thyrotropic hormone, and results in rapid involution of the enlarged gland. Oftentimes a gland that was enlarged five or six times may return to normal size after a month or two of treatment with full doses of desiccated thyroid. If treatment is stopped, the goiter usually recurs.

The requirements of thyroid hormone by an infant or a child are much larger than have generally been supposed, and should not be calculated accord-

ing to the ordinary criteria of weight or age by which dosages of drugs usually are calculated. A newborn infant frequently requires at least 1½ gr. of desiccated thyroid* daily to effect proper involution of a large diffuse goiter showing hypofunctional hyperplasia. Small children tolerate 2 gr. of desiccated thyroid* readily, and children more than three or four years of age usually tolerate full dosages: in effect, 3 gr., and usually require such dosages to obtain desired involution of the gland.

The type of desiccated thyroid tablet given is important because there is considerable variation in the strength of different products. A U.S.P.† standardized brand should be used, and it is important that the desiccated thyroid tablets are *uncoated*, because a coating often interferes with their being absorbed.

(b) *Struma lymphomatosa.* A second form of diffuse goiter that occurs in children is struma lymphomatosa (Hashimoto's thyroiditis). Although in children it is rarely seen in its typical form (with oxyphilia, fibrosis, lymphocytosis, and germinal centers), minor degrees of the same changes, including infiltration of the thyroid with lymphocytes are fairly common. These changes are often described as "lymphadenoid goiter."

The etiology of struma lymphomatosa is not clear. It has recently been suggested by Roitt, Campbell, and Doniach[2] that the basic cause is autoimmunity, with sensitization of the body to its own thyroglobulin. This sensitization is thought to result in the destruction of thyroglobulin by an antibody, and this in turn results in hypothyroidism, in stimulation of the pituitary to increase its output of thyrotropic hormone, and in compensatory hypertrophy and hyperplasia of the thyroid cells. Whether or not this explanation is correct, varying degrees of failure of thyroid function are the rule in struma lymphomatosa, and treatment with full doses (2 to 3 gr.) of desiccated thyroid daily results in suppression of the output of thyrotropic hormone and in shrinkage of the goiter. Usually, after two months of treatment, children's diffuse goiters due to struma lymphomatosa have returned to normal size but, unless a maintenance dose of 1 or 2 gr. of desiccated thyroid is given daily, the goiter is certain to recur.

3. *Nontoxic nodular goiter.* Nodular goiter in children is rare, but sometimes in children who have an extensive family history of goiter or who have congenital goiter or cretinism, large multinodular goiters may develop early. These may be extreme examples of the same diathesis that causes sporadic nontoxic nodular goiter seen in patients in mid-life. The childhood type of goiter appears to be the result of enzymatic defects in the thyroid causing impairment of thyroid function.[1] Most of these multinodular goiters are associated with subclinical hypothyroidism; the hypertrophy of the thyroid, with formation of nodules may take place because the pituitary stimulates the growth of the thyroid or because of a hypersensitive response of certain groups of cells to thyrotropin.[3]

The development of multinodular goiters in children can be prevented and in some cases corrected by administration of full doses of desiccated thyroid. All nodules do not involute in response to such therapy, and sometimes, when the goiters are large enough to be conspicuous, thyroidectomy is indicated.

Thyroid U.S.P., The Armour Laboratories.

†*United States Pharmacopeia.*

Whenever a subtotal thyroidectomy is performed for a nodular goiter in a child or a young adult, the patient should be warned that unless he takes desiccated thyroid in doses of at least 1 or 2 gr. daily, *indefinitely*, the same factors that caused the goiter to develop in the beginning will still cause a new goiter to develop in the remnants of the thyroid. All children operated upon for nodular goiter should, therefore, take desiccated thyroid throughout life to compensate for this permanent inability to synthesize sufficient thyroid hormone.

Since nodular goiters of the type commonly occurring in adults are rare in children, the significance of a thyroid nodule in a child is much greater, from the standpoint of possibility of malignancy, than is a similar nodule in an adult. Most of the nodules of benign multinodular goiters are soft, whereas most carcinomas of the thyroid are extremely hard and appear as solitary tumors or diffuse infiltrations of a part or all of the gland. In children any hard nodularity or infiltration of the thyroid should be viewed with grave suspicion, and in the majority of cases such nodules or areas of infiltration should be removed completely.

4. *Toxic diffuse goiter (Graves' disease)*. Toxic nodular goiter is almost unknown in children, but toxic diffuse goiter (Graves' disease) occurs fairly frequently. When it does occur it is apt to be typical in every respect and associated with exophthalmos, an easily palpable diffuse enlargement of the thyroid, tachycardia, and muscular weakness. Except in the young child, in whom weakness may be the predominant symptom and the child may be suspected of suffering from muscular dystrophy, the diagnosis usually is clear.

Hyperthyroidism in children responds well to treatment with antithyroid drugs, but usually control is maintained only while the antithyroid drug is being given. In my experience prompt recurrences after treatment is stopped are the rule, and the more severe and typical the hyperthyroidism the less apt antithyroid drugs are to effect permanent control of the disease. The choice of definitive treatment lies between administration of radioiodine and preparation with an antithyroid drug followed by subtotal thyroidectomy.

In young children, subtotal thyroidectomy is a satisfactory means of controlling hyperthyroidism, but, because of the small size of the larynx, operation entails a slightly increased surgical risk. In the event of postoperative edema of the larynx, or paralysis of even a single vocal cord, tracheotomy may be necessary. In the hands of experienced thyroid surgeons, this complication should be rare, but in children under ten years of age it is a distinct hazard. Recurrences are fairly common if radical subtotal thyroidectomies are not performed, and if they are, the incidence of hypothyroidism is high. In a series of 21 patients treated by partial thyroidectomy at the Cleveland Clinic Hospital there was recurrent hyperthyroidism in five, and four were rendered hypothyroid.

Another disadvantage of thyroidectomy in children is that regardless of how the incision is made keloids usually develop. For the first year or two these keloids may be disfiguring, but eventually they flatten out into broad and oftentimes conspicuous scars, so that cosmetically, thyroidectomy is not so satisfactory in children as it is in adults.

Administration of radioiodine is a much simpler and probably safer way of treating hyperthyroidism in children. In the past ten years, we have treated

22 children in this way, and in the majority of cases, doses as small as 4 or 5 mc. controlled the hyperthyroidism. In this series, in one patient recurrent hyperthyroidism developed and three patients became hypothyroid.

Since from 80 to 90 per cent of the radioiodine is concentrated in the thyroid, relatively little radiation is received by the rest of the body. For example, after a dose of 4 mc. given to a girl with Graves' disease with a high uptake of I^{131} in the thyroid, the amount of radiation received by the ovaries is on the order of that received in an ordinary gastrointestinal series of roentgenograms. In order to have any effect on menstruation, doses of several hundred millicuries are required as compared to the four or five employed in Graves' disease.

To date there have been no reported cases in which thyroid carcinoma has developed. Experimental work on animals suggests that radiation per se is not carcinogenic in the thyroid unless thyroid function is depressed and the output of thyrotropic hormone is increased. Under these circumstances, radiation can be carcinogenic in animals, but complete protection against the development of benign or malignant tumors of the thyroid of animals can be obtained by feeding the animal desiccated thyroid, and suppressing the abnormal stimulation that otherwise comes from the pituitary.[4] If hypothyroidism develops after treatment with radioiodine it is therefore important that desiccated thyroid be given to maintain normal thyroid balance.

On the basis of all clinical and laboratory evidence now available it would seem that the risk of inducing a fatal carcinoma of the thyroid in a child by giving small doses of I^{131} is considerably less than the intrinsic risk of thyroidectomy.

5. *Cancer of the thyroid.* Although cancer of the thyroid is not common in children, I have, during the past 20 years, treated 18 children who had thyroid carcinoma. Seventeen of the neoplasms were papillary carcinomas or follicular variants of the papillary which behave in exactly the same way as the papillary carcinomas. These tumors are not encapsulated, but involve the surrounding thyroid tissue and metastasize predominantly to regional lymph nodes. In children, papillary carcinoma may also metastasize to the lungs. The only nonpapillary carcinoma of the thyroid which I have seen in a child was in an 11-year-old girl, and it was an encapsulated angioinvasive carcinoma that grossly was indistinguishable from a benign solitary adenoma of the thyroid. The youngest child was three years old at the time of operation for carcinoma of the thyroid; the oldest was 15 years. The age distribution was uniform in the children between these ages. Eleven of the 14 children whose early histories were adequate had roentgen radiation around the head, neck, or thorax when they were infants; three had no irradiation. Six were given irradiation for thymic enlargement, two for eczema, two for enlarged adenoids or tonsils, and one for enlarged lymph nodes.

In only four of the 18 patients with cancer of the thyroid was a nodule in the thyroid the leading sign of the disease. In 14 cases, cervical nodes appeared before a change was detected in the thyroid, and in seven patients, even after the cervical nodes were palpable, the tumor in the thyroid was so small that it was not felt at the first examination. Thus, in nearly half of the patients the

primary tumor was occult. In four patients, pulmonary metastasis occurred before the presence of the thyroid nodule was noticed. Delay in treatment after observation of the first sign of the disease varied from 1 week to six years, but did not seem to have as much influence upon the prognosis as one might expect. Five patients were operated upon less than six months after the first sign of the disease was noted; four of them are well, and one at present has residual disease. Five were operated on more than three years after the first sign of the disease; three of them are well, and two have residual disease. The period of follow-up in the two groups averages four and one-half and five years, respectively. Each of four patients who had pulmonary metastasis before operation had metastasis before the nodule in the thyroid was noticed.

In two patients it is possible that delay in treatment adversely influenced the course of the disease. In the first of these, a five-year-old boy, operation was delayed for a year after the lymph nodes were first noticed, and at the time of operation the primary tumor had invaded the trachea. This was the only locally inoperable cancer in the series. In the second case, the patient waited two years after the appearance of cervical lymph nodes, and roentgenograms of the chest then showed extensive pulmonary metastasis. It is impossible to determine whether earlier treatment would have avoided this complication.

Involvement of lymph nodes was more extensive than in adults. Eleven of the 18 patients had 20 or more nodes involved, four had from 10 to 20, two had from 5 to 10, and it was only in the case of the angioinvasive carcinoma that no cervical nodes were involved. Thus, in contrast to the findings in adults, in whom only 65 per cent of the papillary carcinomas metastasize to regional lymph nodes, all of the papillary carcinomas in this series of children had so metastasized at the time of operation.

The type of papillary carcinoma of the thyroid which occurs in children appears to be susceptible to control by feeding desiccated thyroid, as evidenced by the results of treatment of five patients in this series. The pituitary's output of thyrotropic hormone is suppressed by thyroid and, in the majority of cases this results either in failure of the tumor to grow, or in actual involution of the existing tumor. In view of the endocrine sensitivity of these tumors, it seems unwise to subject children with papillary carcinomas to any form of therapy, such as treatment with I^{131}, that may induce hypothyroidism, and thereby stimulate the tumor to grow.

The 18 children in this group have been followed up to 20 years since operation, an average follow-up period of more than five years. Only four patients have had recurrences in the regional lymph nodes and none has had recurrence in the thyroid area. Three of the four recurrences took place within a year of the first operation and after simple removal of the involved nodes there has been no further recurrence. The operations that have been performed have resulted in no severe dysfunction or deformity. In the 16 operable cases there has been only one case of permanent tetany, and no permanent tracheotomies have been necessary. Most of the operations were done through wide transverse thyroidectomy incisions, and in no case was the sternocleidomastoid muscles resected or the contour of the neck altered.

Sufficient time has now elapsed to make it clear that the combination of an adequate, nonmutilating operation that removes all of the grossly involved thyroid and all of the grossly involved groups of nodes, together with continuance of treatment with desiccated thyroid suffices to prevent local recurrence of the disease. Moreover, distant metastasis has not taken place after operation for any of the operable papillary tumors in this series. Seventeen of the 18 patients are living and none have evidence of recurrence in the neck. The one patient who died had been treated elsewhere by total thyroidectomy, bilateral radical neck dissection, and I^{131}. He came to us with advanced pulmonary metastasis and so much cyanosis and dyspnea that he could not take full doses of thyroid. The four children who had pulmonary metastasis before operation have done well and in each case the metastasis has regressed or has been held in check by feeding of desiccated thyroid. The one child with a nonpapillary, angioinvasive carcinoma is living seven years after operation with no local recurrence but with metastasis to bone. From the results of this form of treatment it appears that it is not necessary to perform mutilating radical neck dissections on children in order to insure protection against local recurrence and systemic spread of papillary carcinoma.

Summary

1. Diffuse nontoxic goiter in children usually is the result either of hypofunctioning hyperplasia of the thyroid or variations of struma lymphomatosa. In either case the patients should be treated by feeding of desiccated thyroid rather than by iodine.

2. Nontoxic nodular goiter is rare in children. Its growth is best prevented by feeding of desiccated thyroid, and can sometimes be corrected by such feeding.

3. Solitary nodules should be removed because of the high incidence of carcinoma in such nodules in children.

4. Graves' disease in children can be treated by subtotal thyroidectomy following preparation with antithyroid drugs or, better, by administration of small doses of radioiodine.

5. Most carcinomas of the thyroid in children are papillary and metastasize to cervical nodes. In three fourths of the cases the enlarged nodes were observed before the thyroid tumor was noticed.

6. Most children with papillary carcinoma of the thyroid can be adequately treated by operations performed through a transverse thyroidectomy incision, which neither deforms the neck nor interferes with the function of its muscles.

7. Eleven consecutive patients having operable papillary carcinoma of the thyroid with no evidence of pulmonary metastasis have been treated in this way and are free of disease up to 20 years following operation.

8. The feeding of desiccated thyroid inhibits the growth of most of the carcinomas of the thyroid that occur in children, and should be given *routinely and indefinitely* after thyroidectomy to all patients operated upon for cancer.

9. For most of the types of goiter that occur in children today, feeding of desiccated thyroid is a much more effective remedy than is iodine.

References

1. Stanbury, J. B., and Querido, A.: Genetic and environmental factors in cretinism: classification. J. Clin. Endocrinol. **16:** 1522-1532, 1956.

2. Roitt, I. M.; Campbell, P. N., and Doniach, Deborah: Nature of thyroid auto-antibodies present in patients with Hashimoto's thyroiditis (lymphadenoid goitre). Biochem. J. **69:** 248-256, 1958.

3. Zondek, H., and Leszynsky, H.: Genesis of thyroid adenomas. Lancet **1:** 77-78, 1956.

4. Bielschowsky, F.: Neoplasia and internal environment. Brit. J. Cancer **9:** 80-116, 1955.

PREOPERATIVE DIAGNOSIS OF SYMPTOMATIC MECKEL'S DIVERTICULUM

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MECKEL'S diverticulum, with an incidence as high as 2 per cent,[1] has been reported to be the most common congenital gastrointestinal anomaly. Nevertheless, mortality from symptomatic diseases of the diverticulum has been reported to be from 6 per cent to 21.6 per cent.[2-5] These high rates have been attributed to delay in diagnosis and in operation.

Concerning the diagnosis of symptomatic Meckel's diverticulum little has been written except in the areas regarding exclusion of other causes of recurrent abdominal pain, peritonitis, intestinal obstruction, or rectal bleeding. The differential diagnosis usually includes appendicitis, mesenteric adenitis, worms, intestinal hemangioma, polyp, food allergy, recurrent intussusception, intestinal duplication, allergic purpura, and anal fissure.

The variety of descriptions of the pain associated with symptomatic Meckel's diverticulum leads one to conclude that periumbilical pain is usual although not pathognomonic. The differential diagnosis between bleeding from the Meckel's diverticulum and some of the more common causes of gastrointestinal bleeding in young patients, such as anal fissure, polyps, intussusception, and duodenal ulcer has been thoroughly described. In an attempt to find the most commonly associated symptoms in patients with proved symptomatic Meckel's diverticulum, a survey of records of patients was undertaken in order to aid earlier diagnosis and operation, and thereby reduce the mortality.

Material

The records of 24 patients in whom the diagnosis of Meckel's diverticulum was proved by operation between 1928 and 1958 comprise the series. All age groups were included in order to provide maximum opportunity for comparison of symptom patterns. The data of the 24 proved and symptomatic cases are summarized in Table 1.

Diagnosis

A correct, presumptive, primary, preoperative diagnosis of Meckel's diverticulum was made in 9 of 24 cases (37.5 per cent). The diagnosis was made as a second choice in two cases.

Preoperative *proof* of the diagnosis was obtained in three of the nine cases. One patient (Case 1) had a congenital persistence of the vitelline duct which, when injected with contrast medium, showed roentgenographic retrograde filling of a Meckel's diverticulum and the terminal ileum. In one patient (Case

Table 1.—*Summary of data* for 24 patients who had symptomatic Meckel's diverticulum**

Case number	Age, years	Sex	Pain			Bleeding		
			Frequency	Site	History	Bouts, number	Transfus., number	Frequency
1	1/6	M	—	—	—	See Comment	0	Daily
2	2	F	—	—	—	2	0	6 mo.
3	3	F	2 mo.	Umb.	1½ y.	3	0	2 mo.
4	3	M	2 mo.	Umb.	2 mo.	2	1	2 mo.
5	3	F	4 w.	Umb.	1 y.	2	0	2 mo.
6	4½	M	—	—	—	1	6	—
7	4½	M	2 w.	Umb.	6 mo.	0	0	—
8	5½	M	1 w.	Umb.	4 y.	0	0	—
9	8	F	1 w.	Umb.	3½ y.	6	12+	6 mo.
10	11	M	2 mo.	Umb.	2 y.	1	2	2 y.
11	11½	F	—	—	—	4	2	2 mo.
12	13	F	1 w.	Umb.	2 y.	2	7	2 mo.
13	19	M	—	—	—	3	4	2 mo.
14	23	M	1 mo.	Umb.	1 y.	5	0	2 mo.
15	28	F	Cont.	Gen.	1 d.	0	0	—
16	31	M	1 d.	R. l. q.	1 mo.	0	0	—
17	45	M	1 d.	R. l. q.	1 mo.	0	0	—
18	49	M	1 w.	Umb.	5 mo.	0	0	—
19	50	M	Cont.	R. l. q.	1 d.	0	0	—
20	50	M	1 mo.	Gen.	15 y.	0	0	—
21	56	M	—	—	—	3	6	1 mo.
22	60	M	1 w.	R. l. q.	4 mo.	0	0	—
23	61	M	Cont.	Gen.	5 d.	0	0	—
24	74	M	Cont.	Epi.	7 d.	0	0	—

*Umb. = umbilical; Cont. = continuous; Gen. = generalized; Epi. = epigastric; G = gastric; I = ileal; P = pancreatic; R. l. q. = right lower quadrant.

Table 1. —*Continued*

Preoperative diagnosis	Emergency operation	Types of mucosa in diverticulum	Ulcer present	Diverticulitis present	Perforation present	Comment
Persistent vitelline duct	No	—	—	—	No	Patent vitelline duct from birth with slight daily bleeding and escape of feces; specimen lost.
Suspected Meckel's diverticulum	No	G I	Yes	No	No	
Meckel's diverticulum; suspected intussusception	No	P G I	Yes	No	No	Acute appendicitis and ileocolic intussusception at age 19 months, Meckel's diverticulum noted but not removed.
Suspected Meckel's divert. and tumor	No	G I	Yes	No	No	
Recurrent intussusception	No	G I	Yes	No	No	
Suspected polyp; Henoch's purpura	Yes	G I	Yes	No	No	
Perforated appendicitis	Yes	G I	Yes	Yes	Yes	
Meckel's diverticulum	No	G I	Yes	No	No	
Suspected Meckel's divert. and polyp	Yes	G I	Yes	No	No	
Suspected Meckel's diverticulum	No	G I	No	No	No	
Suspected Meckel's divert. and polyp	No	G I	Yes	No	No	
Suspected ulcerative colitis and Meckel's diverticulum	Yes	G I	Yes	No	No	
Polyp	Yes	I	Yes	No	No	
Suspected tumor; psychoneurosis	No	I	No	No	No	Symptoms of crampy umbilical pain persisted four years postoperatively; negative roentgen findings.
Acute appendicitis	Yes	I	No	Yes	No	
Ileitis	No	I	No	Yes	No	
Meckel's diverticulum	No	I	No	Yes	No	Only positive radiologic diagnosis; retrograde filling of diverticulum by barium enema.
Chronic pancreatitis	No	I	Yes	Yes	No	Ileo-ileal intussusception with diverticulum as the leading point. Extraluminal mass felt by rectal examination preoperatively.
Ileitis	Yes	—	—	Yes	Yes	Emergency appendectomy done before admission here followed by fecal fistula; resection and ileocecostomy one month later.
Suspected tumor and Meckel's divert.	No	I	No	No	No	Recurrent obstructive symptoms due to peridiverticulitis, fibrosis, and kinking of adjacent ileum.
Duodenal ulcer	Yes	G I	No	No	No	
Incarcerated hernia	Yes	I	No	No	No	Recurrent obstructive symptoms; diverticulum incarcerated in right indirect inguinal hernia and small fibrosarcoma 6 in. proximally.
Sus. gallstone ileus	Yes	I	No	Yes	No	
Sus. gallstone ileus	Yes	I	No	Yes	No	

17) a preoperative barium enema filled the ileum and diverticulum in retrograde fashion. In one patient (Case 3) an operation for appendicitis and ileocolic intussusception had been performed at the age of 19 months, at which time a Meckel's diverticulum was noted proximal to the intussusception, but was not removed. Because of persistence of symptoms of recurrent periumbilical pain and rectal bleeding the diverticulum was removed at a second procedure.

An acute abdominal episode requiring emergency operation occurred in four of the children and in seven of the adults. Signs of peritoneal irritation were present in three, massive bleeding in five, and obstruction in three patients.

The use of various roentgen technics, using contrast media to study the gastrointestinal tract at all levels, was unproductive except in the two patients diagnosed preoperatively as previously mentioned. Long intestinal tubes used to localize the level of bleeding were undependable in four patients, since bleeding had ceased spontaneously in three and the tube could not be passed easily through the duodenum in the fourth patient. Measurement of occult blood in the stool of children whose presenting complaint was abdominal pain was carried out in only one patient (Case 8) and was strongly positive one day following an attack of pain.

Proctosigmoidoscopic findings were negative in all of the pediatric patients who had rectal bleeding. Use of the proctosigmoidoscope in conjunction with the barium enema examination, particularly with the air contrast enema, should be a basic part of the diagnostic procedure for such patients to rule out fissures and polyps.

Operation

In the majority of patients the operation consisted of simple diverticulectomy, by means of division between clamps placed transversely to the long axis of the ileum, at the base of the diverticulum. Closure was carried out in the same axis. In patients in whom it was apparent that this maneuver was likely to narrow the lumen of the ileum, segmental resection and end-to-end or side-to-side anastomoses were used. In each of two patients (Cases 1 and 19) a cutaneous fistula with the diverticulum was removed en bloc. There was no mortality in the group of patients operated on, some of whom underwent late exploration in the presence of the complications of massive hemorrhage, perforation, or obstruction. Relief of symptoms was achieved in all of the patients as determined by follow-up from one week to eleven years.

Pathologic Findings

Pathologic material was available for examination in 22 of 24 cases. The specimen presumably was lost in Case 1. In Case 19 perforation, abscess, and fistula formation had obliterated all vestiges of mucosa lining the muscular remnant of the diverticulum.

Three anatomic varieties of Meckel's diverticulum were seen. In Case 1 a patent omphalomesenteric (vitelline) duct in a newborn infant with pouting umbilical intestinal mucosa bled readily, but not profusely, and allowed the escape of small amounts of intestinal content. In Case 11 there was a diverticulum of the usual position and configuration, but with a solid fibrous cord extending from its apex to the undersurface of the umbilicus. In all of the remaining patients there was the more common form of a diverticulum located from 1½ to 4 ft. from the ileocecal valve, on the antimesenteric border of the ileum, from 1 to 12 cm. in length and from 2 to 5 cm. in diameter.

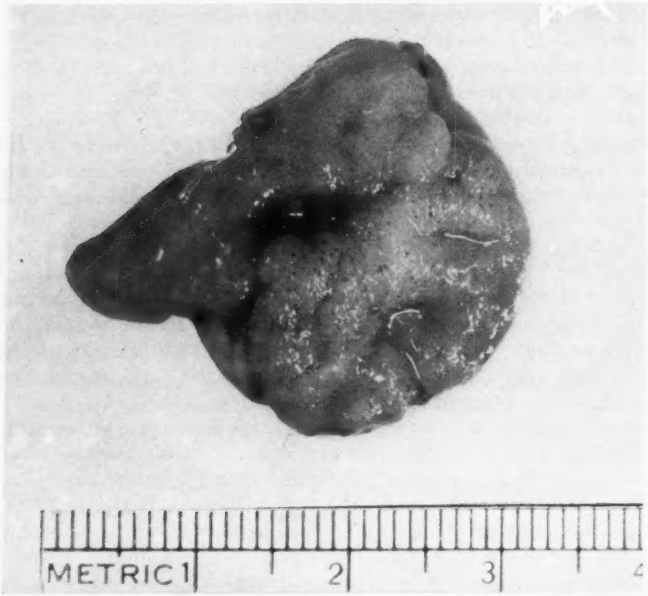
Less common (clinical) presentations occurred in five patients. In two patients (Cases 7 and 19) perforation occurred; in one patient (Case 22) a variation of Littré's hernia was found, the diverticulum being incarcerated in an indirect inguinal hernia with a small fibrosarcoma of the ileum 6 in. proximal to the diverticulum; and in one patient (Case 20) a chronic peridiverticulitis with local fibrosis and kinking of the small bowel produced obstructive symptoms. Intussusception occurred in only one patient (Case 18).

It was not possible to make an anatomical reassessment and accurately correlate bleeding in the absence of ulcer or gastric mucosa. Healing of an ulcer may have occurred by the time of operation in two patients (Cases 10 and 14). The plane of section may have missed a punctate erosion in two patients (Cases 13 and 21), since emergency operations were performed during active bleeding, but no evidence of ulcer was reported. The presence of gastric mucosa in the diverticulum was established in 11 of the 12 children under 15 years of age; there was no record of examination of the specimen in Case 1. Ten of the 12 children who passed blood in the stool had heterotopic gastric mucosa in the diverticulum. In the two children in whom there was no evidence of bleeding, diverticular ulcers were present. In one patient in whom there was rectal bleeding, and gastric mucosa present in the diverticulum, no ulcer was found in the specimen. The typical anatomic association of gastric mucosa with ulceration in the adjacent or opposite wall is shown in Figures 1 and 2. A correlation of anatomic and pathologic findings is summarized in Table 2.

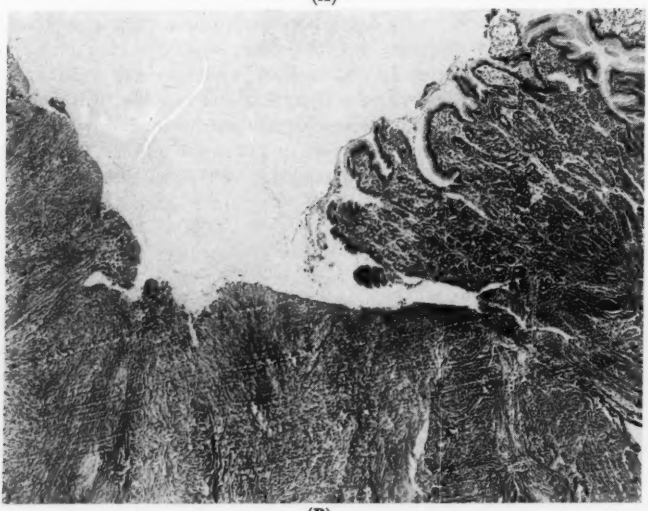
Discussion

The roentgen diagnosis of Meckel's diverticulum is difficult and undependable, as indicated by a recent report[6] in which a survey of the literature yielded only 37 instances of proved preoperative diagnosis in adults. Physical findings are similarly of little value except when peritoneal irritation is present. The symptom pattern and clinical history still appear to be of greatest value in diagnosis.

The symptoms most consistently present in the infants and children with proved symptomatic Meckel's diverticulum in the series discussed here were *pain* and *bleeding*. Four of the 12 children had gross rectal bleeding only, two had pain only, and six had recurrent pain and bleeding. The pain, more adequately described by the older children in this series, usually was crampy, periumbilical, rarely shifting to the right lower quadrant or the infra-umbilical region, seemed

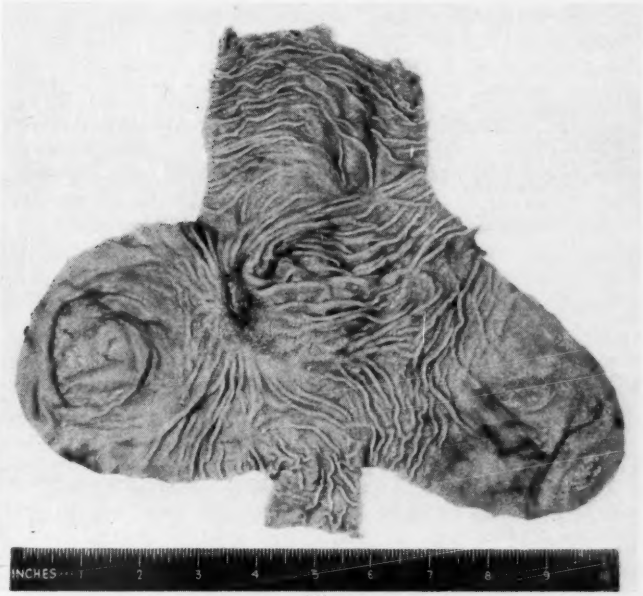


(A)

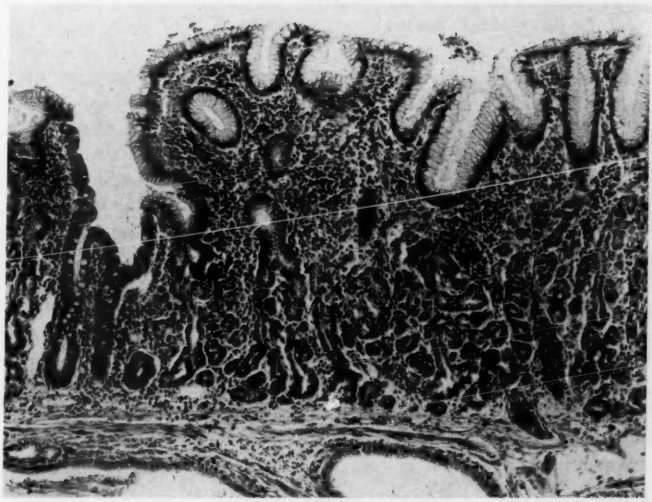


(B)

Fig. 1. (**A**) Photograph of gross specimen showing peptic ulcer in Meckel's diverticulum adjacent to heterotopic gastric mucosa;(**B**) photomicrograph of a section; hematoxylin-eosin stain; x 40.



(A)



(B)

Fig. 2. (**A**) Photograph of gross specimen showing peptic ulcer in Meckel's diverticulum at the base of the diverticulum with heterotopic gastric and pancreatic mucosa in the fundus; (**B**) photomicrograph of a section; hematoxylin-eosin stain; x 40.

Table 2.—*Correlation of anatomic with pathologic findings*

Symptoms	Type of mucosa* in diverticulum	Number of patients	Number of patients who had			
			Ulcer	Diverticulitis	Perforation	Obstruction
Pain	I	8	1	6	0	3
	G I	2	2	0	1	0
	P G I	0	0	0	0	0
	Not known	1	?	?	1	0
	Total	11	3(?)	6(?)	2	3
Pain and bleeding	I	1	0	0	0	0
	G I	5	4	0	0	0
	P G I	1	1	1	0	0
	Not known	0	0	0	0	0
	Total	7	5	1	0	0
Bleeding	I	1	1	0	0	0
	G I	4	3	0	0	0
	P G I	0	0	0	0	0
	Not known	1	?	?	0	0
	Total	6	4(?)	0(?)	0	0

*I = ileal; P = pancreatic; G = gastric.

to be unrelated to meals, was not relieved by eating or the use of antispasmodics or antacids, and in three patients occurred during periods of fasting. One significant characteristic was that the pain occurred in *attacks* of relatively rapid onset, lasting from 1 to 18 hours, and in several patients was associated with audible and visible hyperperistalsis. In none of the patients was positional relief of pain apparent. The characteristic posture was that of any child with severe abdominal pain, the knees drawn up to the abdomen and frequent shifting from side to side. Symptoms of nausea, vomiting, fever, diarrhea, or constipation occurred in various combinations but not in any consistent pattern that would aid in diagnosis. The character of bleeding in these patients was that described by other authors, being typically red with formed clots when bleeding was copious, and red mixed with dark blood when bleeding was less severe. One child showed typical melena with a tarry stool, followed shortly by red blood with clots. This is consistent with the observation by Kiesewetter[5] that some of the blood may be digested by the acid and enzymes formed by gastric mucosa in the diverticulum.

The adult patients exhibited a variety of symptom patterns which occurred for the first time in adulthood and usually were of relatively short duration except for one patient (Case 20), who had recurrent small-bowel obstructive symptoms for 15 years, associated with fibrosis and kinking of the adjacent ileum

by chronic peridiverticulitis. Two thirds of the adults required emergency operations for perforation and fistula, acute diverticulitis, or massive hemorrhage. The absence of mortality in this collected series notwithstanding, the implication is clear that Meckel's diverticulectomy should be performed prophylactically at the time of laparotomy at any age, and particularly in children who have had suggestive symptoms.

The ratio of sexual incidence has been quoted as 3 to 1 in favor of males, a ratio that is true for this report when the total group of 24 patients is considered, but not for the pediatric group wherein the ratio is closer to 1 to 1.

Other pathologic variations that are said to be common, but were not observed in this series, are torsion of the diverticulum, internal hernia with volvulus, and perforation or obstruction of the diverticulum by a foreign body.

In attempting to explain the cause of diverticulitis in patients without heterotopic tissue in the diverticulum, two main factors have been mentioned. The first is the fact that the Meckel's diverticulum is supplied by an end artery that is a branch of the superior mesenteric artery and is, therefore, theoretically more susceptible to the effects of general systemic disease or infection. In the present series of cases, however, recent or concurrent other illness was not reported. The second factor is the increased likelihood that undigested food particles, particulate matter and foreign bodies will lodge in the diverticulum and will evoke an inflammatory response.

The sequence of events leading up to actual peptic ulceration of the mucosa adjacent to heterotopic gastric mucosa is not clear, particularly because of the episodic nature of the symptoms. The elaboration of hydrochloric acid and pepsin by the heterotopic gastric mucosa is well established, as well as the fact that artificial diverticula in the form of Pavlov pouches will cause ileal ulceration.[7-9] The interpretation of this problem in 1931 by Lindau and Wulff[7] has not been significantly changed. It is presumed that the heterotopic mucosa responds to the ingestion of food, but that additional circumstances must be present for the production of enough ulceration to cause pain or bleeding. In Case 12 the pain was usually crampy, but was boring in nature just prior to the two episodes of bleeding. This also was recorded for other patients, and suggests that one reaction to superficial erosion may be that of segmental hyperperistalsis, producing crampy pain; whereas, penetrating ulceration is more likely to cause pain similar to that of a penetrating duodenal ulcer. While local anatomy and puddling of secretions in the diverticulum may play a role, the persistence of symptoms after simple surgical inversion of the diverticulum into the lumen of the ileum, as cited by Hudson,[9] indicates that they are not essential. Several authors[5,7,9-11] have called attention to the fact that since ulceration may occur at the junction of ileum and diverticulum, the blind application of clamps across the base may exclude the bleeding ulcer, leaving it in situ after the diverticulum has been removed. It would seem that if this occurs, bleeding must cease when the inciting cause has been removed, since secondary bleeding after operation was not observed in any patient in this series.

The most consistently occurring symptoms in the patients in this series in the pediatric group were four in number: (1) *attacks of pain*, recurrent, rather than a

vague soreness or discomfort; (2) *periumbilical location of the pain* with local shifting only, and without radiation; (3) either *crampy or boring pain*, not relieved by usual measures short of narcotics; (4) *rectal bleeding* of liquid red blood and clots when the bleeding is copious, dark or black blood followed by larger amounts of liquid red blood, or by the presence of occult blood in the stool following an attack of periumbilical pain.

Summary

1. The data from 24 patients with symptomatic and proved Meckel's diverticulum are presented. The material has been analyzed for symptom patterns that might be helpful in preoperative diagnosis, especially as applied to children.

2. Of the 12 children in the series, pain was the only symptom in two, bleeding the only symptom in four, and both pain and bleeding the predominant symptoms in six.

3. The most common association of symptoms in the children who had symptomatic Meckel's diverticulum was cramping or boring periumbilical pain occurring in attacks in association with gross or occult blood in the stool.

4. There was no mortality in the surgically treated patients in this series.

References

1. Skinner, I. C., and Walters, W.: Leiomyosarcoma of Meckel's diverticulum, with roentgenologic demonstration of diverticulum: report of case. Proc. Staff Meet., Mayo Clin. **14**: 102-107, 1939.
2. Gross, R. E.: The Surgery of Infancy and Childhood: Its Principles and Techniques. Philadelphia: W. B. Saunders Co. 1953, 1,000 p., p. 219.
3. Brookes, V. S.: Meckel's diverticulum in children; report of 43 cases. Brit. J. Surg. **42**: 57-68, 1954.
4. Söderlund, S.: Meckel's diverticulum in children; report of 115 cases. Acta chir. scandinav. **110**: 261-274, 1956.
5. Kiesewetter, W. B.: Meckel's diverticulum in children. A.M.A. Arch. Surg. **75**: 914-919, 1957.
6. Stein, G. N.; Bennett, H. H.; Finkelstein, A.: Preoperative roentgen diagnosis of Meckel's diverticulum in adults. Am. J. Roentgenol. **79**: 815-822, 1958.
7. Lindau, A., and Wulff, H.: Peptic genesis of gastric and duodenal ulcer; especially in light of ulcers in Meckel's diverticulum and postoperative ulcers in jejunum. Surg., Gynec. & Obst. **53**: 621-634, 1931.
8. Kittle, C. F.; Jenkins, H. P., and Dragstedt, L. R.: Patent omphalomesenteric duct and its relation to diverticulum of Meckel. Arch. Surg. **54**: 10-36, 1947.
9. Hudson, H. W., Jr.: Meckel's diverticulum in children; second clinical and pathologic study with a report of thirteen additional cases. New England J. Med. **208**: 525-535, 1933.
10. Womack, N. A., and Siegert, R. B.: Surgical aspects of lesions of Meckel's diverticulum. Ann. Surg. **108**: 221-236, 1938.
11. Waugh, J. M.; Herrell, W. E., and Crumpacker, L. K.: Peptic ulcer in Meckel's diverticulum causing intrinsic intestinal obstruction; report of two cases. Surgery **11**: 385-391, 1942.

SURGICAL TREATMENT OF ESOPHAGEAL ATRESIA AND TRACHEO-ESOPHAGEAL FISTULA IN THE INFANT

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ESOPHAGEAL atresia and the associated fistulas between the tracheo-bronchial tree and the esophagus form a highly significant group of congenital anomalies that is regularly seen in hospitals that have many obstetric and newborn patients. Twenty years ago these lesions were considered interesting but hopeless anatomic curiosities; now they are significant because they are curable. Untreated, this group of anomalies is lethal, whereas successful surgery results in a normally functioning upper gastrointestinal tract. Therefore, it is vitally important that the diagnosis be promptly made. At the present time the two commonest reasons for failure of treatment of this anomaly are the presence of other major anomalies and associated prematurity.

Anatomic Considerations

The embryologic aspects of esophageal atresia will not be discussed here, suffice it to say that interruption of esophageal continuity and fistulous communication between the esophagus and the tracheo-bronchial tree are commonly associated, and all of the theoretically possible combinations of esophageal discontinuity and fistula have been seen clinically. The fistula may extend from an upper blind esophageal pouch to the trachea, from the lower end of the esophagus to the trachea, or both esophageal ends may communicate with the respiratory tract. Esophageal discontinuity varies in length and there may be no fistula to the trachea. Conversely, a tracheo-esophageal fistula may be present without an interruption in esophageal continuity; this is the so-called "H" fistula.

In practice, it is important to know that more than 90 per cent of all patients have one basic form of this anomaly: namely, a blind, upper esophageal pouch, with the lower end of the esophagus communicating with the trachea; thus the trachea and the stomach are connected via the distal esophagus (Fig. 1). In our experience, the next most common form of the anomaly is an "H" fistula.

Diagnosis

Infants who have esophageal atresia usually have typical symptoms that are easy to identify. The infants will be "wet," i.e., will seem to have excessive saliva. With esophageal obstruction, they will be unable to swallow saliva and will aspirate it. Similarly in the presence of an "H" fistula, esophageal contents will cross into the respiratory tract and will precipitate respiratory distress. Also,

in most instances gastric secretions can regurgitate into the respiratory tract. The first attempts at feeding may have rather dramatic consequences. These considerations make it obvious that an alert nursing staff in the neonatal nursery will in most instances be able to suspect the diagnosis. Nursing personnel should, for that reason, be thoroughly educated in recognizing the signs of esophageal atresia and tracheo-esophageal fistula.

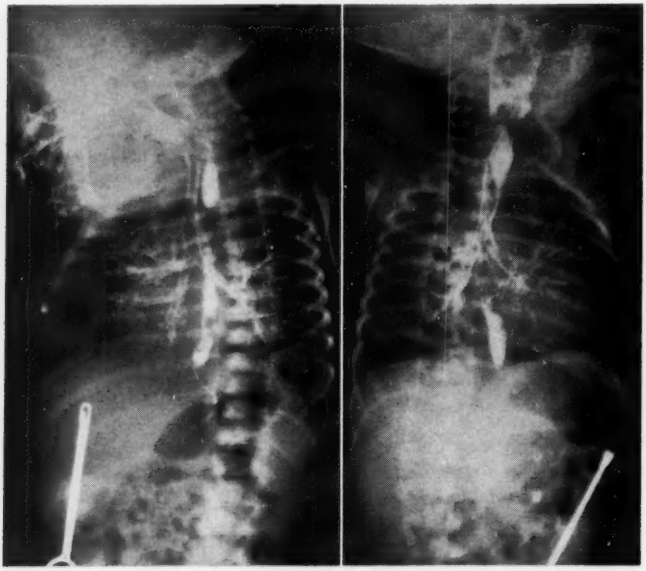

Fig. 1. Roentgen photographs that show evidence of the typical anomaly of esophageal atresia with tracheo-esophageal fistula. The infant in this case had been given more than the usual amount of contrast medium, which resulted in exceptionally clear outlines of the tracheobronchial tree and lower esophageal segment. Note the blind upper esophageal pouch filled with contrast medium; also the lower esophageal segment leaving the mid-tracheal region. There is evidence of considerable gas present in the gastrointestinal tract, which is proof that the distal esophagus communicates with the trachea.

In the usual type of the anomaly the diagnosis is readily confirmed by two procedures: (1) Attempts to pass a catheter into the stomach will be unsuccessful: the tube will "hit bottom" soon after it has passed through the pharynx. (2) If having made this first observation, 1 or 2 ml. of iodized oil are instilled into the catheter, and a roentgenogram is made, the evidence of a blind, esophageal pouch will be present. Frequently this small amount of contrast medium will be sufficient to result in a limited gratuitous bronchogram that demonstrates how easily the infant aspirates when he cannot swallow. Considerable additional information can be obtained from the roentgenograms. In most instances there will be evidence of air in the upper gastrointestinal tract, which proves the presence of the common type of anomaly with communication from the trachea

to the distal esophagus. The tendency for children with this anomaly to aspirate frequently results in pneumonitis, most commonly in the right upper lobe. The severity of the pulmonary changes can be readily assessed from the roentgenograms.

The "H" type of fistula without obstruction sometimes is an extremely difficult diagnosis to make. The fistula is easily overlooked both through the bronchoscope and the esophagoscope. It may be demonstrated by use of contrast medium and roentgenography; however, the presence of contrast medium in both the esophagus and tracheobronchial tree following oral administration of the medium does not indicate necessarily the presence of a fistula (Fig. 2). There

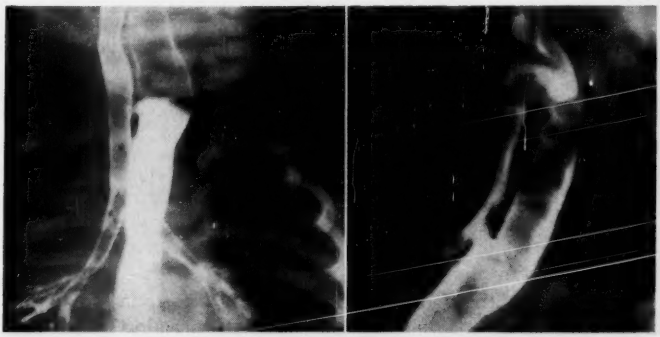

Fig. 2. Roentgen photographs that demonstrate evidence of an "H" fistula. Note that the level of the fistula is above the level of the first rib and thus is actually cervical in location; also, in the view on the right, that the contrast medium not only crossed at the level of the fistula, but also was aspirated through the larynx above.

is a significantly large group of infants with laryngeal and pharyngeal difficulties, usually neurologic, who are prone to aspirate, and whose symptoms may thus be mistaken for those related to fistulas. One of our patients was observed for more than a month before a fistula was conclusively proved by barium swallow and cinefluorography.

Preoperative Preparation

Although esophageal atresia must truly be considered a surgical emergency, it should be stressed that hours consumed in preoperative preparation are well spent. With the usual type of anomaly, the infant will have had no oral intake and, depending upon the time interval since birth, dehydration may be a serious factor. Time also well spent will be that taken to obtain satisfactory toilet of the tracheobronchial tree, and treatment of pneumonitis. However, it must be realized that as long as the condition remains uncorrected, the pulmonary problems will almost surely be self-perpetuating. A valuable maneuver in the preoperative care of the infant is the placement of a catheter on suction in the blind upper esophageal pouch. Continuous evacuation of this pouch in sump-drain fashion will minimize aspiration.

Surgical Technic

Thanks to the visionary surgical pioneering in this field performed by Haight,[1] Ladd,[2] and others,[3,4] the direct anatomic correction of this anomaly has become a well-standardized and dramatically effective operative procedure. In a great majority of instances the anatomy is such that a take-down of the fistula and a direct end-to-end esophageal anastomosis are possible, and result in an anatomically and functionally normal swallowing mechanism.

We have currently been employing a conventional, right, posterolateral, transpleural thoracotomy approach through the fourth intercostal space. There usually is no difficulty in identifying the terminal esophagus and its fistulous communication to the trachea. This fistula is divided flush with the trachea, and the tracheal opening is closed with interrupted, fine-silk sutures. One of the postoperative complications has been the re-establishment of a fistulous communication, and for this reason it is wise to cover the site of tracheal closure with a flap of mediastinal pleura or areolar tissue.

Identification of the blind proximal end of the esophagus is facilitated by the dilatation which is usually present, secondary to the obstruction. It frequently saves time to have the anesthetist pass a soft-rubber catheter into the blind pouch, and exert gentle pressure. This readily demonstrates its position and facilitates mobilization.

Approximation of the two ends of the esophagus for anastomosis may be a problem. Usually, upward mobilization and gentle traction on the upper end with multiple stay sutures, thus converting a short, fat pouch into a long, narrow one, will overcome a deficit in length. The upper end, which may be hypertrophied, is mobilized, in preference to the narrow hypoplastic distal end, mobilization of which conceivably could jeopardize the blood supply. The anastomosis is basically one layer of silk (00000 or 000000 atraumatic) interrupted sutures. Occasionally some of the hypertrophied muscle from the upper end is pulled down over the anastomosis as a second layer. One should carefully avoid using excess sutures, lest they endanger the blood supply or create a diaphragmatic obstruction to the minute esophageal lumen.

It is our current practice after a primary anastomotic operation to thread one of the extremely small, modern, plastic catheters through the anastomosis into the stomach. This has been used initially for aspirating purposes and subsequently for feeding. Although we do not use it, gastrostomy must be entirely satisfactory, as other surgeons use it extensively for gastric decompression and feeding.

Unfortunately, occasionally simple, direct anastomosis is not readily feasible such as when the distal esophageal segment is short or entirely absent. Under such circumstances, the stomach can be progressively mobilized up through the esophageal hiatus, a method that probably is preferred if the upper esophageal end is of good length. Although anatomically feasible, it is technically rather formidable to anastomose the infant's stomach to the esophagus in the neck. If a primary anastomosis cannot be readily accomplished, three things must be done at the time of the initial operative procedure: (1) the fistula must be taken

down; (2) the upper esophageal end must be exteriorized in the neck, creating a salivary fistula so that pulmonary aspiration is avoided; (3) a feeding gastrostomy must be established for alimentation. We currently believe that such an infant should then be maintained on gastrostomy feedings for approximately two years, after which time, in a one-stage procedure, the right colon can be substituted for the esophagus through an extrapleural anterior mediastinal tunnel. Insufficient time has elapsed for us to have completed this operative approach for this particular anomaly, but success in applying this approach to caustic esophageal stricture has been so gratifying that we believe that this course will be more satisfactory than will a high thoracic transplantation of the stomach.

Postoperative Care

Specific problems in the postoperative care of the infants are related to management of the indwelling gastric tube, and to feeding. Infants normally are held in an upright position to be burped after feeding, yet in postoperative management this technic usually is forgotten and the infants are left in a horizontal position until the stomach overflows. Aspiration, or gastric dilatation, becomes a hazard. These difficulties can be avoided if great care is taken to keep the gastric tube patent. This is particularly important in the infant who has had an esophageal anastomosis. Vomiting past one of these minute anastomoses is hazardous for the baby—as well as hard on the surgeon's nervous system! Forty-eight hours postoperatively it has been our custom to initiate intermittent feedings through the indwelling tube. Intermittent feeding seems to be more physiologic than does a continuous drip, and the danger of overfilling the infant's stomach is largely avoided. Also, the tube is open between feedings, so that the baby may burp through it and avoid gastric distention. In our experience, a small plastic tube in the esophagus is well tolerated, and we have been in no hurry to remove it. The tube may have some value in preventing immediately postoperative strictures. However, if the child can swallow around the tube a week after surgery, it should be removed.

The distal limb of the anastomosis is always of extremely small caliber. It is remarkable how it dilates as soon as normal swallowing is restored. However, the anastomosis itself can be no bigger than the distal limb, and it is not surprising that anastomotic strictures frequently occur. We know of no way of predicting in which infant a stricture will develop, and for this reason we now believe that all of these surgically treated infants should have the caliber of the anastomosis checked not less than two weeks postoperatively. This is readily done by passing relatively stiff urethral rubber catheters, starting at approximately size number 10 French. If graduated catheters up to size numbers 16 or 18 can be passed, there seems to be little chance of future stricture. However, it is much easier to prevent a stricture than to dilate a well-established one, and we repeat the same procedure several weeks later, at the time of the first examination after discharge from the hospital. An established stricture usually can be

treated successfully from above; however, at least the first few dilatations should be done under direct vision, treatment that will not be discussed here.

Summary and Conclusions

Esophageal atresia and tracheo-esophageal fistula are related anomalies that occur fairly often in newborn infants. It is stressed that these lesions are surgically curable, congenital defects and, therefore, early diagnosis and prompt treatment are extremely important. The diagnosis can be readily suspected by mere observation of the infant, and nursing personnel should be thoroughly indoctrinated in this regard.

References

1. Haight, C., and Towsley, H. A.: Congenital atresia of esophagus with tracheoesophageal fistula. Surg., Gynec. & Obst. **76:** 672-688, 1943.

2. Ladd, W. E.: Surgical treatment of esophageal atresia and tracheoesophageal fistulas. New England J. Med. **230:** 625-637, 1944.

3. Gross, R. E.: The Surgery of Infancy and Childhood: Its Principles and Techniques. Philadelphia: W. B. Saunders Co., 1953, 1000 pp., p. 75.

4. Haight, C.: Some observations on esophageal atresias and tracheoesophageal fistulas of congenital origin. J. Thoracic Surg. **34:** 141-172, 1957.

THERAPY FOR CARCINOMA OF THE UTERINE CERVIX; PART II: SURGERY

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THE surgical treatment of cervical carcinoma has been subject to a tremendous burst of enthusiasm in the past ten years. Published surgical results might give one the false impression that the use of irradiation has been largely discarded; in Part I we and our associates[1] discussed the importance of irradiative therapy. New surgical procedures have been made possible and old ones have been made safer by improved anesthetics, antibiotics, surgical technics, and an imaginative attitude on the part of surgeons. Some operations are so new that they have not yet been thoroughly evaluated, while other currently accepted operations are being misapplied or poorly executed. Because of these factors it is difficult to delineate precisely the indications and contraindications for the use of surgery.

This report concerns only invasive carcinoma of the uterine cervix. Carcinoma in situ is purposely excluded because we believe that that lesion represents an entirely different condition in many cases. We agree wholeheartedly with the suggestion of Blaikley, Kottmeier, Martius, and Meigs[2] that carcinoma in situ be omitted from the clinical classification of carcinoma of the cervix. Although it does represent a major cellular abnormality, in many cases it is not a clear-cut entity. In most instances carcinoma in situ is amenable to local treatment if certain precautions in diagnosis and follow-up are observed. Our experience with an approach to the diagnosis and treatment of carcinoma in situ has been recently reported.[3]

The surgical treatment of invasive cervical carcinoma requires facilities and abilities for highly specialized technics. When operative intervention is contemplated, the surgeon should be prepared to carry out the most extensive procedure necessary to cope with the disease, and should in no way compromise the patient's future well-being by lack of technical ability or ancillary facilities. The most complete laboratory and technical facilities must be available. Successful radical surgery demands not only the co-operative efforts of an anesthesiologist, a pathologist, and a gynecologist, but also the assistance of any surgical or medical specialist whose particular talents might conceivably be needed in the care of the patient. This care includes the preoperative, operative, and postoperative phases. These operations demand the utmost in team cooperation and should not be undertaken when any of the above facilities are substandard or are lacking.

Operations for Cure

Operative procedures that are undertaken with cure in mind, consist of the radical hysterectomy (as opposed to the Wertheim hysterectomy), and the three

exenteration procedures (anterior, posterior, and total). *Simple total hysterectomy is contraindicated in the treatment of invasive cervical carcinoma (either alone or in combination with irradiation).*

In no case, should a radical hysterectomy be undertaken unless the surgeon is capable of extending the scope of the operation to any of the exenteration procedures if the extent of disease makes one of them desirable. These are precise, refined, surgical procedures that can be done with relative safety and surprisingly small blood loss when the surgical team is experienced.

Radical hysterectomy with bilateral dissection of deep pelvic lymph nodes is the most precise and oftentimes the most difficult of the above operations to perform, in that selected structures are removed with considerable risk of damage to remaining viscera. Ureterovaginal or vesicovaginal fistulas may result from direct trauma or devascularization, and severe bleeding may occur during the dissection of the lateral pelvic walls. This operation involves a complete removal of the broad-ligament tissues, a complete dissection of the fat and the lymph nodes of the lateral pelvic walls, complete visualization of the pelvic course of the ureters, removal of the upper portion (one fourth to one third) of the vagina with the paravaginal structures, as well as removal of the uterus, the tubes, and the ovaries. This operation should be distinguished from the classic Wertheim operation that involves only an extensive hysterectomy without dissection of lymph nodes.

In theory, radical hysterectomy is not a good operation for cancer of the uterine cervix because the ureters so closely approximate the cervix. This anatomic feature makes it necessary to cut across potentially cancer-bearing tissue in the process of the operation. Furthermore, substitutes for the bladder are not as yet sufficiently satisfactory to justify removing the bladder as a standard procedure thereby overcoming this problem.

Anterior exenteration involves the removal of the bladder in conjunction with a radical hysterectomy and dissection of the lymph nodes. *Posterior exenteration* combines removal of the rectum and the lower sigmoid colon with a radical hysterectomy; whereas, *total exenteration* involves the removal of both the rectum and the bladder together with the uterus, the tubes, and the ovaries. The anterior and the total exenterations have been used most frequently in treating cervical carcinoma, and each involves the use of a substitute bladder. The substitutes that have been devised are illustrated in Figure 1 (A–D); the most widely employed bladder substitute is at present the Bricker's pouch. With the construction of a Bricker's pouch, an external urinary opening still is necessary, and if the rectum is removed there is a separate colostomy. We do not favor the transplantation of ureters to a sigmoid colostomy because the so-called "wet colostomy" is difficult to control and often is extremely distressing to the patient. Chronic pyelonephritis with azotemia is a common complication.

We have recently devised an operative procedure that we hope will overcome the necessity for external ostiums except as temporary measures (Fig. 2). This involves performing a total exenteration from an anterior approach and the preservation of a short rectal stump. A low anterior intestinal anastomosis, with a temporary transverse colostomy, is done. A Bricker's pouch is also constructed.

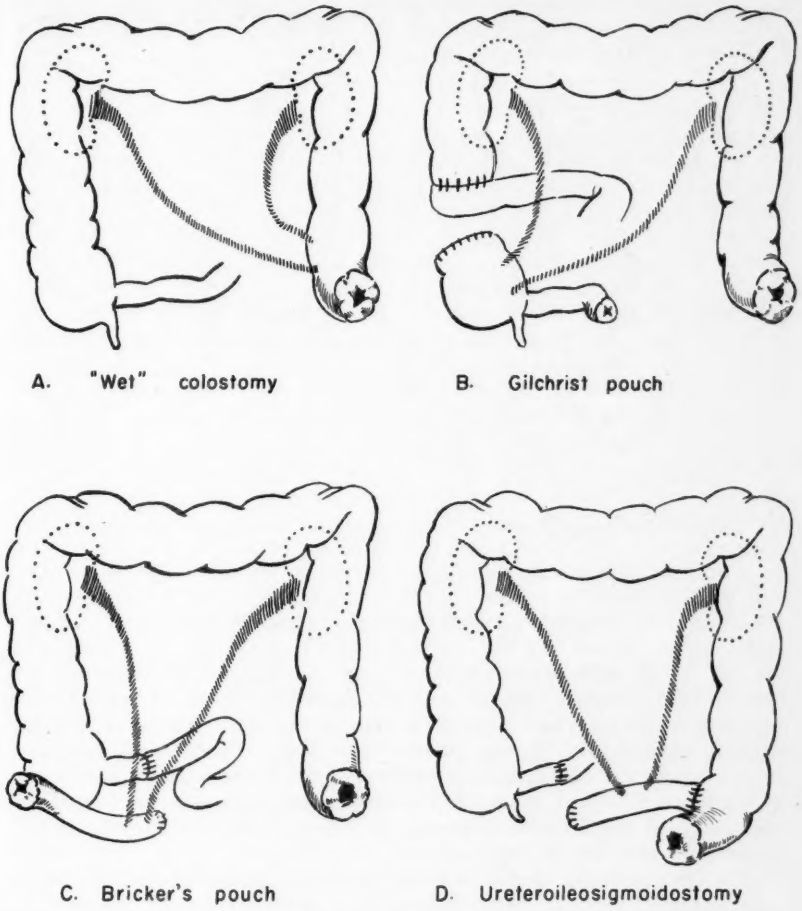

Fig. 1. Bladder substitutes.

When convalescence has proceded to a suitable extent, the transverse colostomy is closed. At a later date the Bricker's pouch is inserted into the sigmoid colon and the abdominal stoma is closed. A series of primary ureteroileosigmoidostomies for congenital urinary problems has been previously reported in this journal.[4] The results have been satisfactory to date. One patient who has had a total exenteration is now waiting to have the Bricker's pouch transplanted to the sigmoid colon.

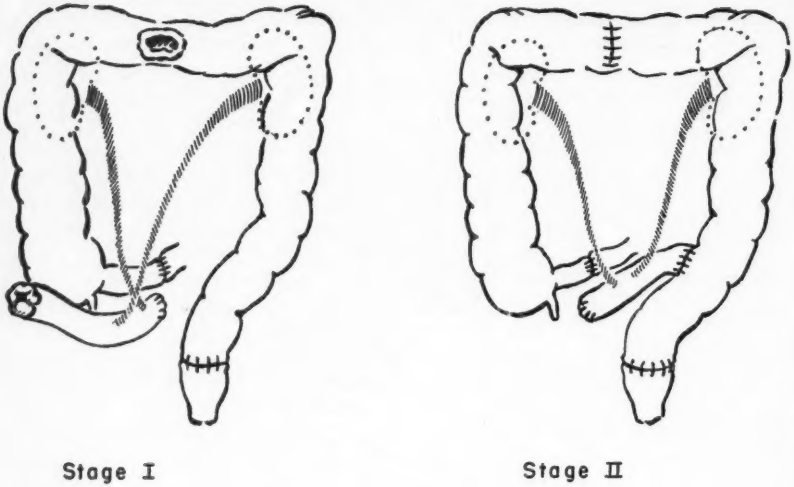

Fig. 2. Ureteroileosigmoidostomy with low anterior rectosigmoid anastomosis.

Operations, Indications, and Contraindications

The precise indications for curative, radical, surgical procedures are not entirely clear, although some contraindications have become apparent. We generally reserve the radical hysterectomy for the early carcinoma that has failed to respond to irradiation. An early case is one that is for the most part confined to the cervix with possibly minimal extension to the vaginal wall or the broad ligament. Where there is disease lateral to the cervix, it occasionally is possible to perform a radical hysterectomy, but more often an anterior or total exenteration is indicated.

For the occasional carefully selected patient the immediate risk of surgery may be preferable to the delayed sequelae of irradiative therapy. These latter complications are definite and may constitute a real threat to the future good health and emotional adjustment of the patient. Vaginal atresia and shrinkage with attendant coital problems is one of the major considerations in addition to irradiative cystitis, proctitis, and damage to the small bowel. With this in mind we occasionally use radical hysterectomy with dissection of the lymph nodes for primary treatment of stage I and early stage II lesions.

Exenteration procedures are employed when radical hysterectomy is infeasible because of extensive disease, also as primary therapy when there is evidence of extension of carcinoma to or through the bladder or the rectum. Rarely exenterations are used for severe, debilitating sequelae of irradiation when there is no evidence of active malignant disease.

The contraindications to the exenteration operations are fairly obvious: serious systemic disease, evidence of extension beyond the confines of the true pelvis, or involvement of the nerves or of the vessels of the pelvis. In order to make these determinations it is often necessary to carry out extensive preoperative evaluation but, more importantly, operability may not be determined until the abdomen is explored. Unfortunately, in rare instances surgical procedures are undertaken and partially completed before it becomes apparent that the lesions are not completely resectable. If preoperative roentgen studies indicate a favorable situation, the patient should have the benefit of exploration despite a seemingly "frozen" pelvis, because a radical operation still may be possible. The condition of the legs may contraindicate operation, swelling may be due to lymphatic obstruction; pain may be due to nerve involvement. These assumptions often can be confirmed by careful rectovaginal examination, but, when this is not possible, pelvic exploration should be carried out.

The exenteration operations are too new to be completely evaluated, for while it is true that a certain percentage of patients can and do survive the operation and carry on an active and happy life, free of disease, there is a larger percentage who die as a result of extrapelvic recurrences and complications of their disease. Reported operative and hospital mortalities are high. The primary problem is that despite care in selection of patients we do not know enough of the individual variations and the host responses to carcinoma to determine intelligently in advance those patients who will benefit from such operations.

The emotional impact of extensive operations has been somewhat overemphasized. It is true that there may be a definite psychologic reaction to the loss of normal bladder, rectal, and vaginal function, but most women can make a satisfactory adjustment even to a permanent ileostomy and colostomy if they are free from disease and able to carry on an otherwise normal life.

We have been performing exenterations in carefully selected private patients since 1951. They are patients who must finance the lengthy hospitalization and frequent complications incurred in extensive surgery. The care of these patients is time consuming. The operations often are prolonged exercises in surgical technic. Many of these patients have seen savings and economic resources melt away under the impact of long-endured chronic illness and previous extended medical care. For these reasons, we have made every attempt to avoid using these operations for the purpose of palliation.

In the past seven years, we have performed 18 anterior or total pelvic exenterations; we have not employed the posterior exenteration for cervical carcinoma. Of the 18 patients, seven are still living from eight months to six and one-fourth years after the operation; 11 died of their disease in from five months to three and one-half years after the operation. There have been no operative or immediately postoperative deaths in this group. We believe that this is largely a result of the team effort that employs the abilities of the urologist, the colon surgeon, the gynecologist, and all other medical or surgical specialists who are most capable of managing various aspects of operative and postoperative care. Early in the series we used ureterosigmoidostomy for a substitute bladder, but in the past five years we have almost exclusively constructed the Bricker's pouch (Fig. 1C.)

In the same seven years, 20 patients underwent radical hysterectomy, all of whom have survived from 7 months to 5 years and 10 months after operation. Nineteen patients are clinically free of disease; one patient has extensive disease. From 1951 to the present time, 539 patients with various stages of cervical carcinoma have been examined here.

From the above figures it is apparent that our criteria for the selection of patients for more radical operative procedures have been exceedingly rigid. We have not been performing surgery just for surgery's sake. We have adopted a conservative approach to the problems presented and have attempted to avoid radical palliative procedures that only serve to palliate the surgeon's conscience or the patient's family.

Operations for Injuries from Irradiation

A second use of surgery is in the treatment of sequelae of irradiation in the absence of demonstrable residual carcinoma. It is generally true that progressive ureteral obstruction is indicative of advancing carcinoma, but there is a distinct group of patients in whom the obstructive changes are secondary to irradiation. These lesions can be treated in various ways depending on the nature of the problem and the extent of the damage. Neoureterocystotomy (reimplantation of the ureter into the bladder), ureterosigmoidostomy, and construction of the Bricker's pouch each have been used as corrective measures.

Irradiative lesions in the large bowel are most often on the anterior rectal wall opposite the cervix, where the maximal amount of irradiation has been given or where radium has been misapplied. Fistulation or stricture may occur, making a colostomy necessary in either case. On rare occasions only a temporary colostomy is needed in order to allow the stricturing and ulcerating process to subside or to effect a repair of the fistula. Rectal resections with "pull-through" should not be attempted because of extensive postirradiative scarring at this site and the danger of reactivating the carcinoma, also the area usually is so severely devascularized by previous irradiation that primary healing may not occur.

Irradiative injuries to the small bowel may be localized or diffuse. Localized changes occur when a loop of bowel is adherent in the pelvis and is exposed to the full impact of irradiation. When an isolated injury from irradiation occurs it may result in a low-grade or a complete obstruction or, in rare instances, perforation may follow. Diversionary procedures are employed in preference to local resections because there is generally a fairly diffuse microscopic reaction to irradiation involving much of the small bowel. By carrying out a lesser procedure there is less danger of delayed or incomplete healing.

Vesicovaginal fistula occasionally results from faulty placement of radium or too vigorous irradiation. An operative repair of the fistula may be feasible but often there is so much reaction that a diversionary operation is the only recourse. The Bricker's pouch or ureterosigmoidostomy is more easily controlled by the patient than is a cutaneous ureterostomy.

Operations for Palliation

Palliative operations can be divided into four categories according to their specific purposes: (1) relief of pain, (2) correction of urinary fistulas and, occasionally, obstruction; (3) correction of intestinal obstruction or fistulation; (4) control of bleeding.

The type of operation employed for the relief of pain depends on the nature and distribution of the pain. Cordotomy is frequently employed and may be either unilateral or bilateral. After a unilateral cordotomy the opposite side also often must be operated upon to obtain complete relief of pain; intense pain on one side of the body may mask significant pain on the contralateral side. Subarachnoid injections of alcohol may be used to control pain in the sacral area. Each of these operations carries with it a risk of interfering with the mechanism of micturition, a problem easily solved by the use of an indwelling catheter. Prefrontal lobotomy, presacral neurectomy, and caudal anesthesia have been suggested but are not frequently used because the above-mentioned methods of relief of pain have been found to be more effective and predictable. Cobalt-60 teletherapy has decreased the need for operative precedures for relief of pain.

Major urinary operations seldom are indicated for palliation. Obstruction of the urinary tract and resulting uremia is a common cause of death in uncontrolled cervical carcinoma. Death results from coma and its complications, and is pain-free. Any attempts to relieve the uremic coma add to the patient's discomfort and, if successful, result in a more protracted painful terminal illness.

Urinary fistulas present a real problem in nursing care, and because of this are worthy of correction if the patient can reasonably tolerate surgery. The simplest procedure consistent with correction of the problem is generally employed; most often it consists of nephrostomy or cutaneous ureterostomy. On rare occasions, if the rectum is uninvolved and the rectal sphincters are competent, ureterosigmoidostomy may be undertaken.

The major indication for palliative intestinal surgery is the existence of an enterovaginal fistula. It generally is corrected by simple sidetracking operations. Intestinal resections are neither indicated nor necessary. Colostomy seldom is used as a primary palliative procedure once obstruction has occurred. However, occasionally when an exploratory operation is performed and curative surgery is not possible, impending rectal or sigmoid obstruction is recognized. In this situation a transverse or descending colostomy may be done. Seldom is palliative colostomy indicated for a rectovaginal fistula.

Irradiation has been effective in preventing exsanguination, thereby decreasing the need for surgery. However, when surgery must be used for the control of bleeding, the ligation of the internal iliac arteries may be lifesaving. This operation can be carried out either transperitoneally or retroperitoneally.

Surgical Exploration

Abdominal exploration has not been utilized to its optimal extent in the past. The reluctance to employ this diagnostic tool has been understandable in

that not too long ago this procedure involved considerable risk to the patient. However, even with the most up-to-date diagnostic methods, we often are unable to determine without operation the true extent of the patient's disease. All experienced physicians remember an occasional patient for whom the prognosis seemed utterly hopeless, yet at exploration a benign condition or a correctable malignancy was found. Knowing the true extent of malignant disease also permits more realistic planning of palliative therapy. A carcinoma can be so advanced that no curative treatment is possible and yet still be for the most part confined to the pelvis. This, however, is an entirely different situation from that presented by a disease that has spread to the liver or to the periaortic lymph nodes in the upper abdomen. In the case of carcinoma confined to the pelvis, the use of palliative irradiation or surgery may be reasonable because of the patient's considerably longer life expectancy. In the case of carcinoma in the upper abdomen, the patient's only need is sympathetic symptomatic medical care.

Several years ago one of us[5] suggested the use of the so-called "second-look" operation in managing malignant pelvic lesions. The second-look consisted of re-exploration of the abdomen at an arbitrary time after the completion of the irradiative therapy or after operation performed in the hope of cure. Now we believe that such operations have little to offer since it is impossible by mere inspection to determine the presence of microscopic involvement of lymph nodes. By the time that gross nodal metastasis is evident, survival rates have declined to zero. However, we do believe that because of the inadequacy of present diagnostic methods we should not hesitate to perform an exploratory operation if there is clinical suspicion that carcinoma persists after irradiative therapy. This approach is important in detecting persistent or recurrent disease in the central pelvis before metastasis to the lymph nodes makes curative operations impossible. We can no longer sit back complacently and watch patients after irradiative treatment—we must be vigorous in our attempts to detect the failure of irradiation at an early stage.

Summary

Surgery may be used for curative, diagnostic, or palliative purposes in patients having carcinoma of the uterine cervix. If a curative operation is contemplated, the surgeon should be capable of performing and have the necessary ancillary facilities for the most extensive surgical procedures. A brief review of our experiences with curative surgery is presented. Various palliative procedures have been outlined and a plea has been made for wider use of abdominal exploration where reasonable doubt exists either as to the extent of the patient's disease or to her response to irradiation. We believe that in most instances a well-planned and integrated course of irradiative therapy should be used primarily in the treatment of cervical carcinoma, and that surgery should be reserved for the so-called "irradiative failures."

References

1. Krieger, J. S.; Zeit, P. R.; Sindelar, P. J., and Hays, R. A.: Therapy for carcinoma of uterine cervix; part I: irradiation. Cleveland Clin. Quart. **25**: 121-124, 1958.

2. Blaikley, J. B.; Kottmeier, H. L.; Martius, H., and Meigs, J. V.: Classification and clinical staging of carcinoma of uterus; proposal for modification of existing international definitions. Am. J. Obst. & Gynec. **75**: 1286-1291, 1958.

3. Krieger, J. S., and McCormack, L. J.: Indications for conservative therapy for intraepithelial carcinoma of uterine cervix. Am. J. Obst. & Gynec. **76**: 312-319; discussion, 319-320, Aug. 1958.

4. Turnbull, R. B., Jr., and Higgins, C. C.: Ileal valve pouch for urinary tract diversion; preliminary report of eight cases. Cleveland Clin. Quart. **24**: 187-192, Oct. 1957.

5. Krieger, J. S.: Surgical approach to cervical carcinoma. Cleveland Clin. Quart. **21**: 27-30, 1954.

MANAGEMENT OF ACUTE CHOLECYSTITIS

Analysis of 67 Consecutive Cases

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General Considerations

ACUTE cholecystitis is essentially a surgical problem. Nearly all cases begin as the result of the mechanical action of gallstones, either by obstruction of the cystic duct or by erosive action on the wall of the gallbladder. Bacterial invasion almost invariably is secondary to the mechanical factor and may occur a matter of days after the onset of symptoms, or not at all. Removal of the gallbladder and its contained stones effects a cure.

It would seem that once the disease has begun and the diagnosis has been established, the therapeutic aim should be prompt cholecystectomy. Yet case anaylses show that delay in surgery is the rule rather than the exception. Further, many internists and family physicians and some surgeons record their belief that operations should *not* be performed during an acute phase of the disease, and that symptoms should be permitted to subside completely; elective cholecystectomy is then to be performed during a quiescent interval some weeks or months thereafter. It is our belief that in most instances substantial delay is not justified and may result in needless suffering, prolonged loss of the patient's time from productive activity and, occasionally, in the development of otherwise avoidable complications.

What are the arguments advanced by those who favor procrastination?

1. "*Most attacks of gallbladder pain subside spontaneously and promptly.*"

It is true that the average attack of gallbladder colic—almost always the precursor of acute cholecystitis—will last only a few minutes or an hour or two, or will disappear after the administration of a narcotic. It is also true that the borderline between "colic" and "acute cholecystitis" is a hazy one. Perhaps the clinician's thinking would be clarified by the establishment of some arbitrary definitions to aid in the approach to therapy. If pain has not completely disappeared within six hours of onset, the clinician should assume that he is confronted with acute cholecystitis and he should regard his patient as a candidate for urgent operation. The same may be said if symptoms recur a

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few hours after they have been relieved. Though attacks of gallbladder colic commonly subside promptly, there are enough exceptions to this rule to reduce its clinical effectiveness.

2. "*The diagonsis is not always clear, and nonsurgical disease may be producing the symptoms.*"

Often previous roentgen studies will have shown the presence of gallstones, or the gallbladder will have failed to be visualized with the "double-dose" technic. If such a patient should develop mid-epigastric or right upper quadrant pain, tenderness over the region of the gallbladder, and constitutional evidences of an inflammatory process such as fever, tachycardia, or leukocytosis, acute cholecystitis may be presumed without further diagnostic study. However, when these signs and symptoms are present, but there never has been roentgen proof of gallstones or nonfilling of the gallbladder, the problem is different. Here, further diagnostic procedures are in order to avoid a possibly useless operation. The first step is to obtain a plain film of the abdomen; in 10 per cent of patients with gallstones there is sufficient calcium in the stones to cast a characteristic shadow without the use of contrast medium. The evidence of stones will confirm the diagnosis and justify prompt operation.

If the "scout film" does not show stones, diagnostic delay to permit cholecystographic studies is fully justified provided that the patient's general condition permits. It is our practice to give such a patient a double dose of oral contrast medium (to avoid the necessity of repeating the test the following day) and, if clinical suspicion runs high, tentatively to schedule the patient for operation immediately after the interpretation of the cholecystogram. If stones are demonstrated or the gallbladder fails to be visualized, operation is performed. If the roentgen findings show the gallbladder to be normal, surgery is canceled and further observation with additional diagnostic studies is undertaken.

For the patients who are unable to take the oral contrast medium or who will vomit the pills, intravenous cholecystographic studies may be substituted, with suitable allowance of time for the gallbladder to fill. If the intravenous contrast medium cannot be given because of drug sensitivity, the patient's general condition must then be the sole guide to therapy.

It has been argued that cholecystographic contrast media taken orally may actually precipitate an attack of acute cholecystitis, or aggravate an existing one. The evidence supporting this argument is scant, and the counterposition may be taken that even if aggravation of symptoms does occur, this will clarify the diagnosis, and in any event is taking place under careful scrutiny, in the hospital, where it could hardly result in any material harm to the patient.

3. "*Technical difficulties are increased when surgery is attempted on the so-called 'hot' gallbladder, and, by implication, the chances for a surgical miscue.*"

With modern operating room facilities the well-trained surgeon is fully able to cope with the increased technical difficulty presented by an acutely inflamed gallbladder. The operation may be characterized as one that is "hard on the surgeon but easy on the patient."

In the first place, the surgeon has always available the expedient of performing a cholecystostomy: emptying the gallbladder of stones and inserting

a tube for decompression. This will invariably relieve the acute attack. Cholecystostomy normally is succeeded three or four months later by a secondary cholecystectomy, since otherwise re-formation of stones and more attacks will follow. Cholecystostomy will not be necessary in the great majority of patients, but in the extremely ill it may be a lifesaving measure that can be carried out with minimal anesthesia; it may also be the wisest course for the surgeon to follow in patients in whom the usual landmarks have been totally obscured by local inflammation.

In the average patient, however, cholecystectomy will be perfectly feasible. It usually is best to decompress the gallbladder first so that it may be grasped more readily by instruments, and it nearly always is wisest to remove it from the fundus down, performing the dissection millimeter by millimeter until the cystic vessels and the cystic duct are encountered and are ligated. Bleeding from the gallbladder fossa nearly always will subside with light packing and pressure from a malleable retractor, although it is prudent to be prepared for a possible blood transfusion.

In most instances it will be possible to obtain an operative cholangiogram; this should be made since a small proportion of patients with acute cholecystitis will also have stones in the common bile duct (5 per cent in our series). In some patients the inflammatory process will be so severe that cholangiography will be difficult, and exploration of the common bile duct unwise. The surgeon must always exercise caution to avoid excessive pressure while injecting the contrast medium into the common bile duct, lest infection present in the bile ducts be disseminated further. On more than one occasion we have seen a gangrenous gallbladder "come off" in the surgeon's hand without either recognition or ligation of the cystic vessels or the cystic duct; there evidently had been thrombosis and the duct had been obliterated. In such cases it is highly unlikely that stones are present in the common bile duct, and it is better for the patient if the surgeon contents himself with a simple removal of the gallbladder.

Although the surgery of acute cholecystitis is usually more difficult than routine gallbladder operations technically, if the surgeon observes the precautions noted and, above all, is willing to perform an occasional cholecystostomy, no additional danger should accrue to the patient; and if the operation does present technical problems, experience has shown that it takes months for the inflammation to subside sufficiently to make an interval operation much simpler. During this waiting period, on the assumption that operation should be performed only when the disease is in a quiescent phase, another attack is more than likely to supervene, raising the same problems that arose with the first one.

Analysis of Cases

In reviewing cases to see whether they fulfill diagnostic criteria for acute cholecystitis, certain difficulties become apparent. The histopathology of the

removed gallbladder presents problems unlike those in acute appendicitis. Commonly, the gallbladder has had repeated bouts of inflammation, and an acute attack is superimposed on chronic changes in the wall. It is not an uncommon experience for the surgeon to find a tensely distended gallbladder, with a thickened wall, containing "white bile," the so-called "hydrops," in a patient who is essentially asymptomatic at the time of operation. Grossly, such a gallbladder may be indistinguishable from the acutely inflamed gallbladder in a patient experiencing severe symptoms. The microscopic pattern may verify the clinical impression that the condition is indeed chronic. The converse, however, may not be the case; occasionally, such a gallbladder in a patient who has pain and fever, and tenderness over the gallbladder area, also will show no acute inflammation histologically. Hence, the microscopic diagnosis of acute cholecystitis cannot be regarded as the final, arbitrary factor in establishing the diagnosis of the acute episode. It is best to depend on a correlation of the clinical picture presented by the patient, and the gross findings at operation as well as the microscopic picture.

In a consecutive personal series (S. O. H.) of 363 cholecystectomies (excluding incidental cholecystectomy performed in the course of another operation, such as gastric resection for ulcer), 100 cases were regarded as possibly qualifying for study as acute cholecystitis. This number was reduced by eliminating 28 cases in which there was no record of recent pain or the pain was present longer than a week prior to admission to the hospital. All of these 28 patients had gallstones, and in eight the pathologic diagnosis was "chronic recurrent acute cholecystitis," qualifying them from histologic evidence as "acute;" in two patients the pathologic diagnosis was hydrops. Six of the eight who showed acute inflammation in the removed gallbladder had had symptoms from 8 to 29 days, and perhaps could be regarded clinically as representing a "subacute" phase of the disease. Five additional cases were excluded either because both pain and tenderness were absent (three cases) or the pain or tenderness was so located that the gallbladder could hardly have been responsible; one patient of this group showed acute inflammation microscopically. Since all of these patients survived postoperatively their exclusion does not affect the over-all findings or conclusions.

The 67 patients classified as having acute cholecystitis all had the onset of upper abdominal pain a week or less prior to hospitalization, and in most of them the pain was localized to the right upper quadrant or the epigastrium; all but three showed appropriate abdominal tenderness at the time of admission. (In an occasional obese patient with a deeply placed gallbladder protected by an overhanging liver, local tenderness may be absent; in most cases, however, fist percussion over the lower ribs alternately on both sides will elicit a characteristic difference in sensation between right and left, the jar being noticeable to the patient on his right side even though the discomfort is not severe.)

Forty patients had at least a degree of fever, and only 12 had a normal temperature. Leukocytosis seemed to be correlated to the presence of fever, so that only two of the patients with normal temperature had a leukocyte count greater than 10,000 per cu. mm. On the other hand, the microscopic findings

included acute inflammatory changes in all of the 12 patients with normal temperature, confirming the clinical and operative impressions.

Of the 67 patients there were 39 men and 29 women. This contrasts with a ratio of 3 women to 1 man in the remainder of this series. Perhaps the apparent discrepancy may be explained on the basis that men are more likely to refuse cholecystectomy for the mere presence of stones and an occasional short bout of colic, and a serious complication is necessary before they leave their jobs to enter the hospital. The age span in this group ranged from 25 to 75 years, both extremes represented by women.

Pathologic Findings

In all but three patients gallstones were present. In these three the pathologic report was "chronic recurrent acute cholecystitis"; in two there was a positive culture, and in the third there was a coexisting (and possibly causative) acute pancreatitis. One of the two patients with a positive bile culture had a cyst of the common bile duct, presumably congenital. Three of the 64 patients having stones in the gallbladder had stones in the common bile duct as well, although the incidence is considerably lower for this group than in the elective group (where in our experience it is more than 20 per cent). Nevertheless, it would seem that cholangiography is warranted, when it can be safely and conveniently done, to avoid secondary operations. Furthermore, if the gallbladder is acute cholecystitis should be stoneless, "reflux" cholecystitis as a result of common bile duct obstruction from a stone, or pancreatitis with inflammation resulting from the reflux of pancreatic juice into the gallbladder, should be looked for via cholangiography. Although a single large stone can produce an "erosive" cholecystitis and it takes only a single small stone to obstruct a cystic duct, 50 of the 64 patients with stones had multiple stones.

The histopathologic diagnoses listed by the pathologist were as follows (biopsies were performed in those patients having cholecystostomy):

Diagnosis	Number of patients
Chronic recurrent acute cholecystitis	43
Acute cholecystitis—	16
(with gangrene 4)	
(with perforation 1)	
Granulation tissue (abscess)	1
Chronic cholecystitis—	7
(with hydrops 1)	
Total	67

As previously noted, the absence of acute inflammation microscopically does not negate the clinical diagnosis of acute disease. In at least one patient

the clinical picture was that of a continuing colic without actually producing the total obstruction usually seen.

Cultures of the bile were made in 55 of the 67 patients. The culture was sterile in 34 instances, confirming the well-known belief that in its initial stages the inflammation is of *mechanical*, not of bacterial, origin. The commonest organisms cultured were, *Escherichia coli* (seven patients), *Staphylococcus albus* (seven patients), and nonhemolytic streptococci (four patients). A higher incidence of positive cultures might have resulted if the wall of the gallbladder rather than the bile had been cultured.

Treatment and Results

Of the 67 patients, 61 were treated by primary cholecystectomy; one patient died in the hospital.

Case 1. A 70-year-old white woman, was admitted to a medical service here because of progressive difficulty in walking, pains in the legs, and gallstones. There was a marked language barrier. She was seen early in the hospital course by the surgical consultant because of an attack of abdominal pain, and right upper quadrant tenderness seemed to be present. Nonsurgical treatment of the symptomatic gallstones was urged in view of the uncertain nature of the basic disorder, presumed to be neurologic. Various studies did not clarify the diagnosis, and since the patient continued to have attacks of severe pain, operation was carried out two weeks after the patient was first admitted. At operation the gallbladder was seen to be large, tense, and thick-walled; in its distal portion a large calculus obstructed the cystic duct. Cholecystectomy presented no special difficulty and operative cholangiograms showed a normal common bile duct. Pathologic diagnosis was chronic cholecystitis.

Postoperatively, the patient did not do well because of progressive generalized weakness and pulmonary complications. She could not cough effectively and ultimately bronchopneumonia and atelectasis developed which failed to respond. Repeated bronchoscopies were carried out in an effort to clear the respiratory passages, but she died 12 days after the operation, and 25 days after hospital admission. Postmortem examination revealed for the first time that the basic neurologic disorder was amyotrophic lateral sclerosis and the progressive weakness led to the fatal outcome. Although judgment could be criticized for operating on this patient, she did present a continuing problem in biliary tract pain, and death, although doubtless hastened by surgery, was due primarily to other causes.

Of the 61 patients having cholecystectomy, cholangiograms were made in 46, and 11 of these underwent an exploration of the common bile duct in addition; stones in the common bile duct were present in two. (The third patient having a stone in the common bile duct underwent primary cholecystostomy). Cholecystostomy was performed in six patients. One of these patients died shortly after readmission 16 days after his operation and three days after his initial discharge.

Case 2. A 65-year-old white man was admitted as an emergency at 4 a.m. with severe epigastric pain that began four days previously and was associated with vomiting. On

physical examination there was a rectal temperature of 101°F., a pulse rate of 96, and a tender mass in the right upper quadrant. An electrocardiogram showed atrial fibrillation. Despite supportive measures with gastrointestinal siphonage, intravenous fluids, and antibiotics, and including digitalization, his condition worsened and, approximately 10 hours after admission to the hospital, a cholecystostomy was performed under intercostal procaine hydrochloride block. The gallbladder was tense and the dome was a mottled, purplish red. When the gallbladder was opened, thin, bloody fluid first escaped, followed by dark, thick bile. The mucosal lining of the gallbladder was shaggy, but no stones were found. A biopsy showed acute cholecystitis, in part necrotizing. A catheter was placed in the gallbladder and the abdomen was closed. A culture of the bile was sterile.

The postoperative course was uneventful except that cholecystocholangiograms demonstrated a calculus impacted in the cystic duct. The patient ran a low-grade fever for a few days but had been normal for 48 hours at the time of his discharge on the thirteenth postoperative day.

Three days later, 16 days after the cholecystostomy, he was readmitted moribund, with no blood pressure or pulse obtainable. A few hours earlier he had severe substernal pain. Despite all efforts at support he died several hours after admission. A postmortem examination showed that death was due to massive thrombosis of portal, splenic, superior and inferior mesenteric veins, infarction of proximal jejunum, and necrosis of the right lobe of the liver. It was believed that this was a coincidental fatal disease occurring after an otherwise satisfactory convalescence. Although the calculus had caused the acute cholecystitis and was not removed at operation, it did not seem to be in any way related to the massive mesenteric thrombosis.

The principal indication for cholecystostomy in these patients was the coexistence of other constitutional infirmity or disease that rendered a prompt relief of symptoms with minimal anesthesia desirable. We believe that a planned cholecystostomy is always justifiable in poor-risk patients; we also believe that it may be resorted to without hesitation or apology whenever in the surgeon's opinion local operative conditions, such as intense inflammation, poor exposure, or a poorly taken anesthetic, render it desirable.

"Early" Versus "Late" Operation

The physician in most instances cannot control the time in the course of the disease when he first sees the patient, and hence often cannot recommend or perform an "early" operation. Table 1 indicates the duration of symptoms at the time the patients entered the hospital, and the elapsed time between onset of *symptoms* and operation. "Early" operation is clearly impossible for those patients who enter the hospital more than two days after the onset of symptoms, but it is still possible for the physician and the surgeon to reduce the hospital stay by avoiding further unnecessary delay.

Table 2 shows that hospital delay may seem excessive even when the policy is to operate promptly. Twenty-five per cent of the patients in this series were operated upon more than five days after entering the hospital.

Table 1.—*Correlation of duration of symptoms from time of onset to hospitalization and to operation for acute cholecystitis in 67 patients*

Total time from onset of symptoms to hospitalization	Total number of patients	Total time from onset of symptoms to operation, number of patients					
		24 hours or less	2 days	3 days	4 days	5 to 7 days	8 days or longer
24 hours or less	27	4	9	3	0	6	5
2 days	9	0	0	3	1	3	2
3 days	9	0	0	0	6	2	1
4 days	5	0	0	0	4	1	0
5 to 7 days	17	0	0	0	0	4	13
Grand Total	67	4	9	6	11	16	21

Table 2.—*Delay in hospital—elapsed time from hospital admission to operation, cumulative figures*

Hospital delay	Number of cases	Percentage
More than—		
5 days	16	24%
4 days	21	31%
3 days	25	37%
2 days	34	51%
1 day	56	34%
Within one day	11	16%

Summary and Conclusions

Acute cholecystitis in most instances is caused by the mechanical action of gallstones and is curable by cholecystectomy. The initiating factor is obstruction of the cystic duct, or mucosal erosion, by the gallstones. Bacterial invasion is secondary and late. Prompt surgical intervention is indicated once the diagnosis is established. In the sick or elderly patient, or in the patient in whom inflammatory changes render the operation unusually difficult, the surgeon should not hesitate to perform a cholecystostomy.

Data from series of 67 surgical patients having acute cholecystitis are reviewed. There were two deaths but, after complete postmortem study, they did not seem to be directly related either to the disease or to the operative procedure.

BLOOD CULTURES FOR DIAGNOSIS OF BACTEREMIA

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THE diagnosis of bacteremia can be made with certainty only after a positive blood culture has been obtained. However, the clinical usefulness of a report on blood culture, whether positive or negative, depends upon the effectiveness of the technic employed in making the culture. In view of the importance of the blood culture procedure in clinical medicine it is surprising that none of the standard laboratory manuals, with the exception of that of Schaub, Foley, Scott, and Bailey,[1] offer more than a cursory description of the technic. Schaub and Foley and their newer collaborators have given an excellent account of their method of blood culture. While their method and our method are in some ways different their procedure also gives good results.

The procedure of blood culture used in our laboratory is a simple one and has been in use many years. Our results have been remarkably accurate, and although we do not use one of the recently devised "closed-system" procedures[2] to prevent contamination, nevertheless our contamination rate is minimal.

Blood Culture Procedure

Three principles. In preparing for a blood culture study, three important steps must be taken: (1) utilizing a technic that minimizes contamination; (2) providing the best conditions for bacterial growth, so that any microorganisms that are present in the blood may have an opportunity to grow; (3) rapidly reporting results so that the physician will be able to use the information while it still is clinically essential, and before it becomes merely a bit of data to be added to the patient's chart.

Preventing contamination. The blood culture method we use permits the growth of any bacteria that may be present, as evidenced by the many positive cultures that are obtained in tubes that have been inoculated with 0.5 ml. or less of blood. The bacteria that are responsible for the contamination of blood cultures come from the air of the room, and from the skin, and the flora of the nose and throat of the patient, of the technicians, and of the other persons in the vicinity. It is well for the technician and the patient to avoid speaking, sneezing, or coughing while the blood is being drawn and inoculated into the culture tubes. Oral spray may contaminate the syringe and, thus, transmit bacteria into the culture medium. In a similar fashion a cotton plug from a culture tube held too near to the operator's face may become contaminated.

Skin organisms can be controlled by scrupulous care on the part of the technician in preparing the site for puncture. The skin disinfectant we use is made up of one part of 2 per cent tincture of iodine, and nine parts of 95 per cent ethyl alcohol. A weak solution of iodine is used because it is light in color

and does not obscure the vein and, although bactericidal, it will not burn the skin. Indeed, the concentration of iodine is so low that it is not necessary to remove excess iodine after the specimen for culture has been taken. The iodine solution on a cotton ball is carefully applied to the center of the field and in the place where the needle actually will penetrate the skin. By beginning in the central area and working outward, the cotton swab is first used at the site of actual puncture, when the swab is clean and uncontaminated by bacteria that it is likely to pick up as it is drawn over the skin.

Sites for puncture. Ordinarily venous blood is cultured, but in some diseases, as in brucellosis, a definitive culture more often may be obtained from arterial blood or from bone marrow. In line with the present interest in microtechnics, especially for children, claims have been made of the usefulness of cultures of capillary blood obtained from a puncture in the heel. It is said that 0.5 ml. of blood obtained from the heel provides satisfactory cultures with minimal contamination;[3] we have had no personal experience with this technic. Several years ago it was suggested that it was feasible to culture petechiae of patients with meningococcal infections, in an effort to recover meningococci from the blood.[4] We have had no personal experience with this technic, but believe that it might be useful under appropriate conditions.

Culture of bacteria. To provide optimal conditions for bacterial growth, and thus obtain the highest incidence of valid positive cultures, it is necessary to draw the specimen of blood at the time that the maximal number of bacteria may be present in the peripheral circulation. This is generally thought to be the period during which the patient's fever is highest. Unfortunately, the laboratory technicians are not always summoned at the optimal time for drawing blood. Most clinicians order blood cultures at such times, but the order occasionally comes for a *stat.* culture to be made for a newly admitted patient whose temperature is normal, but who did have a high fever the night before. Furthermore, although in all probability the patient again will have an elevation of temperature in the afternoon, sometimes it is not feasible to wait that long for a specimen for culture because a course of antibiotics must be started immediately. Such cultures have very little chance of success. One circumstance that has contributed to the high incidence of successful blood cultures in our institution is not only that the laboratory is given the choice of selecting the time to draw the specimen, but also the clinicians whenever possible without danger to the patient make an effort to delay administration of antibiotic therapy until the specimen has been drawn and, if practical, until a definitive blood culture report is available.

Further attempts to provide optimal environmental conditions for pathogenic bacteria that may be present in a blood specimen must center around the culture media used. Many media have been advocated and continue in use. For many years our laboratory successfully used a dextrose infusion broth containing a few small pieces of calf brain.[5]

Since 1942 we have been using a commercially manufactured thioglycollate

medium* because it is simple to prepare and effective. This medium is available in the dehydrated form and may be made by dissolving the dried mixed ingredients in water. The formula is:

Yeast extract	5.0 gm.
Pancreatic digest of casein	15.0 gm.
Dextrose	5.0 gm.
Sodium chloride	2.5 gm.
L-cystine	0.75 gm.
Thioglycollic acid (or sodium thioglycollate)	0.3 ml.
Agar	0.75 gm.
Distilled water	1,000 ml.
Added just before the above ingredients are autoclaved—	
Sodium citrate	3.0 gm.
Para-aminobenzoic acid	0.05 gm.

Thioglycollate, dextrose, and l-cystine are reducing agents and serve to keep the medium in a highly reduced state. When dispensed in culture tubes of 200 mm. by 25 mm., less than 1 cm. of the upper layers of the medium is sufficiently oxidized to give color to methylene blue or other similar oxidation-reduction (Eh) indicators. The culture tubes are filled with the medium to a depth of about 125 mm. Because of the presence of such potent reducing agents as thioglycollate and l-cystine, it is not necessary to use rubber stoppers or oil seals, even for anaerobic cultures. In addition, there is a sufficient Eh gradient within the culture tube so that, regardless of their free-oxygen requirements, the various species of bacteria can find the location that is optimal for growth. The medium is available with or without an Eh indicator. The supply of medium is used rapidly in our laboratory and there is no need for an indicator to determine whether or not oxidation has taken place. Furthermore, we do not use the medium with indicator dye because of the possible bacteriostatic effects that such a chemical may produce.

The presence of the small amount of agar makes the medium sufficiently viscid so that the bacteria develop as colonies rather than as individual bacteria diffused throughout, as in broth medium. Thus, these colonies may be fished out of the culture medium to be stained and subcultured into other media for identification. Many organisms that form easily discernible colonies in the thioglycollate medium fail to grow on blood or on other agar plates unless they first are subcultured through another tube of thioglycollate medium. Agar also serves to prevent diffusion of oxygen from the air throughout the medium.

Para-aminobenzoic acid is added to the medium before it is autoclaved, as it acts as a growth factor and as a specific antagonist of sulfonamides in the blood, if the patient has been treated with any of this group of drugs. Sodium citrate is added at the same time, as an anticoagulant to prevent clotting of the blood after it has been added to the medium. Blood cultures made with clotted

*This medium is available from the Baltimore Biological Laboratory as Thioglycollate Medium Without Indicator, Brewer-modified (No. 01-135C); and from the Difco Laboratories as Bacto Thioglycollate Medium Without Indicator (B430).

blood often are objectionable because the clot binds the colonies of bacteria, which then become difficult to isolate. One or two marble chips dropped into each culture tube will neutralize excess acid that might result from bacterial growth.[6] Penicillinase must be added aseptically to the prepared and sterilized medium and is used only when the patient has a history of penicillin therapy. Penicillinase is not a really effective agent. It may inactivate the penicillin present in the blood but can do little to restore vitality to pathogenic organisms already damaged by penicillin.

Equipment and method. A conventional culture tube is preferable to a prescription bottle or a French square. The narrow neck of a bottle has certain theoretical advantages in regard to minimizing contamination from the air when the container is opened for any reason, but a uniformly wide container, with straight sides, offers a greater advantage when it is necessary to fish for a colony from the depths of the medium. Culture tubes have an added advantage over bottles, in that they occupy less space in the incubator and may be packed more easily in racks or wire baskets, and a number of them may be handled as a unit rather than as individual bottles.

In making blood cultures it is our practice to inoculate each of three thioglycollate-medium tubes with from 1 to 3 ml. of blood. After the blood has been drawn, the needle is removed from the syringe and the blood is expressed directly into the culture tubes. Care must be taken to avoid putting excessively large amounts of inoculum into the medium, because of the bacteriostatic action of fresh blood. Once the blood is in the culture tube, the cotton stopper is replaced without flaming the tube.

The question of flaming the mouth of the culture tube before and after inoculation has been the subject of some controversy.[7] Most technicians still flame the mouth of the tube immediately after removing the cotton or other stopper, and again after inoculating the tube and before replacing the stopper. This has certain theoretical advantages, but in practice it prolongs the time that the culture container is open, and thereby increases the risk of contamination. Frequently it is dangerous to use an open flame near to patients in oxygen tents or in the operating room. The alcohol lamp is a poor substitute for the Bunsen burner, and in order adequately to heat the tube, more care must be taken than usually is practicable. The alcohol lamp has been omitted from our technicians' trays since 1932, and contamination, as mentioned before, has been minimal.

Of great importance to the success of the blood culture is the amount of blood used as inoculum. Human blood when used in large amounts may actually inhibit the development of organisms in the blood culture. Many technics have been developed to overcome this action, since in the past an adequate blood culture was obtainable only when using as large an aliquot of the blood as possible. One technic, used for a number of years, required 50 ml. of blood in 500 ml. of culture medium. This was cumbersome and expensive and, in addition, was unsuccessful and resulted in a comparatively small number of positive cultures.

The cultures are incubated at 37°C. (98.6°F.) and are examined daily to detect possible growth. Care is taken not to agitate the culture tubes, because

many of the bacteria responsible for subacute bacterial endocarditis do not grow diffusely, but rather in the region of diminished oxygen supply. Only if diffuse growth is noted, are smears made from the upper regions of the medium. The zones in and above the erythrocyte layer should be carefully inspected for flaky or granular particles. A sterile pipet should then be lowered into this granular stratum and smears made from the material thus obtained. Negative cultures are examined daily for a minimum of two weeks. Positive cultures on patients who are free of antibiotics almost always show growth within 48 hours. The medium is not recommended for brucella. When brucella organisms are anticipated, a tryptose or trypticase soy bean medium* is used in Casteneda bottles.[8]

References

1. Schaub, Isabella, G.; Foley, M. Kathleen; Scott, E. G., and Bailey, W. R.: Diagnostic Bacteriology; A Textbook for the Isolation and Identification of Pathogenic Bacteria and Systemic Fungi. Ed. 5, St. Louis: C. V. Mosby Co., 1958, 388 pp., pp. 45-49.
2. Scott, E. G.: Practical blood culture procedure. Am. J. Clin. Path. **21:** 290-294, 1951.
3. Correlation of Clinical and Chemical Observations in the Premature Infant; a Working Manual for Physicians and Chemists. Compiled and edited by Natelson, S.; Crawford, W. L., and Munsey, F. A. 2d printing. Rockford, Ill., 1952, 123 pp., p. 107.
4. Smith, D. T., and others: Zinsser Bacteriology. Ed. 11, New York: Appleton-Century-Crofts, Inc., 1957, 953 pp., p. 310.
5. Rosenow, E. C.: Studies on elective localization; focal infection with special reference to oral sepsis. J. Dent. Res. **1:** 205-267, 1919.
6. Haden, R. L.: Elective localization in eye of bacteria from infected teeth. Arch. Int. Med. **32:** 828-849, 1923.
7. Conner, Viola, and Mallery, O. T., Jr.: Blood culture; a clinical laboratory study of two methods. Am. J. Clin. Path. **21:** 785-788, 1951.
8. Ruiz-Castaneda, M.: Practical method for routine blood cultures in brucellosis. Proc. Soc. Exper. Biol. & Med. **64:** 114-115, 1947.

These media are available from the Difco Laboratories as Tryptose Broth (B62) *and from the Baltimore Biological Laboratory as* Trypticase Soy Broth (No. 01-162).

"ESSENTIAL HEMATURIA"—AN OBSOLETE TERM

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THE term "essential hematuria" was coined to denote a condition in which the etiologic factor eludes detection. The definition of essential hematuria as cited in *Dorland's Illustrated Medical Dictionary*[1] conveys the impression of a clinical entity, for it states: "essential hematuria, hematuria for which a cause cannot be determined." To imply to our medical colleagues the existence of such an entity is fraught with danger, when incontrovertible proof of such a disease remains a nebulous uncertainty.

As years have elapsed since the introduction of the expression in urologic nomenclature, it has been employed to describe the condition of patients with hematuria of undetermined origin, although case reports themselves may reveal lack of a complete, comprehensive, general diagnostic survey. An accurate appraisal of this so-called entity in more recent years permits seasoned conclusions to be quoted without the fear of one's being designated a disputative philosopher.

Progress in clinical medicine and research, enhanced by the ever-restless inquisitiveness of the investigator and by curiosity concerning the sciences, has gradually and subtly been rewarded by clarification of the etiologic factors responsible for hematuria. Yes, the term "essential hematuria" is sinking into the opalescent sea of the unknown.

The diagnostician's inability to ascertain the contributing factor or factors responsible for the production of renal bleeding is, unfortunately, oftentimes due to sins of omission. Even as our medical colleagues, all too frequently, fail to evidence the fervid enthusiasm of urologists for complete urologic survey (preferably at the time that the patient observes blood in the urine), similarly, we urologists in many instances inadequately appreciate the labyrinthian courses of general medical diagnostic procedures necessary to establish an accurate diagnosis. Whereas in our urologic armamentarium the diagnostic procedures utilizing cystoscopy, retrograde pyelography, aortography, air insufflation, cineradiography, pneumostratigraphy, and needle biopsy usually permit visualization or detection of the organic lesions associated with hematuria, if they be present, at times because of the minute size of the lesions, detection by any means is rendered difficult, indeed impossible.

We all have been rewarded by the unalloyed satisfaction in certain instances in which, after a period of time has elapsed, re-examination of the patient disclosed the responsible organic lesion. As implied previously, so-called "essential hematuria" is not an autonomous disease, but frequently a symptom or manifestation of general disease.

De Assis[2] has admirably covered the origin of the term "essential hematuria." He has stressed that inflammatory disease of the kidney, acute and chronic intoxications, vascular disease, deficiency disease, and blood dyscrasias may play

From a paper presented at the International Congress of Urology, Stockholm, Sweden, June 25, 1958.

important roles in producing blood in the urine. In my experience, the presence of blood dyscrasias is frequently overlooked. The role of blood diseases such as leukemia, hemorrhagic purpura, and hypoprothrombinuria is well recognized and is widely accepted. Unquestionably, additional blood dyscrasias will be added to the list, for, as recently as 1948, Abel and Brown[3] were the first to report on the incidence of gross hematuria occurring in a patient with sickle cell disease.

Numerous reports in the literature cite lesions of the blood vessels as a cause of gross hematuria.

The histologic examination of the renal tissue should not be a cursory study limited to a few sections. Only a meticulous, painstaking search will, at times, reveal the lesion, and thereby prevent subsequent criticism from being leveled at the urologic surgeon because he has removed a normal kidney.

At this International Congress of Urology, it is time to pause, to reflect, and to decide whether or not a so-called "entity" rests on unshakable foundations or should be relegated to oblivion. One recently published medical dictionary[4] does not list it. Certainly, useless phraseology should be discarded by urologists. I thoroughly concur with De Assis[2] in the statement: "Essential hematuria is obsolete terminology and should be entirely abandoned." This is the *dextro tempore*.

References

1. Dorland's Illustrated Medical Dictionary. 23d ed. Philadelphia: W. B. Saunders Co., 1957, 1598 pp., p. 598.

2. De Assis, J. S.: From a paper presented at the International Congress of Urology, Stockholm, Sweden, June, 1958; publication pending.

3. Abel, M. S., and Brown, C. R.: Sickle cell disease with severe hematuria simulating renal neoplasm. J.A.M.A. **136:** 624-625, 1948.

4. Blakiston's New Gould Medical Dictionary. Edited by Hoerr, N. L., and Osol, A. 2d ed. New York: McGraw-Hill Book Co., Inc., 1956, 1463 pp.

DEDICATION

OF

THE ROBERT S. DINSMORE SURGICAL PAVILION AT CLEVELAND CLINIC HOSPITAL

September 6, 1958

We are gathered here today for the dedication of a dream that is working. Forty-one years ago in an army tent in Rouen, France, Doctor Crile, Senior, Doctor Lower, and Doctor Bunts first dreamed this dream.

In the next 30 years, many surgeons contributed to the dream—Tom Jones, Bill Mullin, Jim Dickson, George Belcher, Ted Locke, Bud Waugh. It was these men, the surgeons they worked with or trained, and the men and women in other departments of the Clinic, who laid the foundations of the dream that is now a reality. All have contributed, but it was Bob Dinsmore who had the inspiration, the foresight, and the genius to project and to design this surgical pavilion.

Many of us questioned the wisdom of making this operating suite so large—22 operating rooms seemed too many. That was five years ago, when it seemed as though antibiotics had conquered the once-surgical problems of infection, and the use of radioisotopes was supplanting thyroidectomy in the treatment of hyperthyroidism. That was also the time when the great development of ultraradical surgery for cancer seemed to have reached its peak. Was this the time, we wondered, to devote 35,000 square feet of the new hospital to operating room space?

While we wondered, Bob Dinsmore went right ahead with the plans. And what happened? New fields of surgery developed. The thoracic surgeons attacked the diseases of the heart. The neurosurgeons injected the basal ganglia to control Parkinson's disease by chemopallidectomy. The otolaryngologists developed the stapes mobilization operation for the correction of deafness from otosclerosis. The urologists learned to recognize hypertension due to blockage of the renal arteries, and devised operations for its correction. Surgical diagnostic procedures became safer and were more frequently employed. Surgeons learned better ways to make ileostomies, and better ways to operate on ulcerative colitis so that ileostomies could be avoided, with the result that more

patients accepted surgical treatment of this disease. Plastic surgery perfected its technics and was more widely accepted. All of this has taken place in the past five years and, most important for the future, the vascular surgeons developed a direct attack on arteriosclerosis.

Doctor Dinsmore was right. In 1957 and in 1958 we have done the largest number of operations in our history. But contrast the type of operations done today and the number of men doing them with the situation in 1924, the year that the hospital was opened. I have here copies of the largest daily operating schedule of 1924 and of 1958. On December 5, 1924, six surgeons performed a total of 35 operations, 19 of which were thyroidectomies. On August 15, 1958, 20 surgeons performed 66 operations, including 58 different types of operations, but only two thyroidectomies. Today the commonest single operation is stapes mobilization for otosclerosis; 358 such operations were performed last year. Last year more than 200 arterial grafts were done, more than 200 operations on the heart, more than 200 resections of the colon or rectum. Most of the commonest types of operations today never had been done in 1924.

The dream moves on. The magnificent success of arterial grafting suggests that as yet we have only a glimpse into the promises of the future. Already it is possible by injecting tissues into an animal before or immediately after birth to condition that animal to receive homografts from an unrelated donor. Already kidneys have been transplanted between identical twins, corneas have been transplanted and, in animals, homografts of glandular tissues have been successfully established in tissue chambers and in the brains of unrelated hosts. It has been found that the injection of tissue extracts, administration of cortisone, or irradiation of the entire body may prolong the survival time of homografts. If we can continue along these lines and break through the immunologic barrier that separates each one of us from the other, the solution of many of our problems may be found. But when that day comes, and when immunologic reactions are no longer our masters but our slaves, it may well be that the doors of this pavilion will be forever closed. To eliminate the necessity of surgery is the surgeon's dream. We hope that we shall live to see that dream come true.

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RECENT PUBLICATIONS BY MEMBERS OF THE STAFF

BRITTON, R. C.: Management of bleeding from the esophageal varices. Connecticut M. J. **22**: 537-542, July 1958.

BROWN, C. H., and DAFFNER, J. E.*: Regional enteritis. II. Results of medical and surgical treatment in 100 patients. Ann. Int. Med. **49**: 595-606, Sept. 1958.

BROWN, C. H., and HASERICK, J. R.: Acute peptic ulcer after triamcinolone therapy; report of three cases. A.M.A. Arch. Dermat. **78**: 289-292, Sept. 1958.

CORCORAN, A. C.: Research in Progress. Voluntary agencies and research support. Bull. Acad. Med., Cleveland: 19-20, 22. Sept. 1958.

CORCORAN, A. C., and PETERS, J. H.†: Editorial. Tenfold in ten years. Circulation **18** (pt. 1): 515-518, Oct. 1958.

CRILE, GEORGE, JR.: Lectureships. Problems in the treatment of cancer. Maryland M. J. **7**: 467-471, Sept. 1958.

CRILE, GEORGE, JR.: The case for conservatism in operations for cancer. Surg. Clin. North America: 1215-1220, Oct. 1958.

CRILE, GEORGE, JR.: Thyroiditis; Method of George Crile, Jr., M.D. *In* Current Therapy, edited by H. F. Conn. Philadelphia: W. B. Saunders Co., 1958, pp. 371-372.

DAFFNER, J. E.*, and BROWN, C. H.: Regional enteritis. I. Clinical aspects and diagnosis in 100 patients. Ann. Int. Med. **49**: 580-594, Sept. 1958.

DUSTAN, HARRIET P., SCHNECKLOTH, R. E.; CORCORAN, A. C., and PAGE, I. H.: Effectiveness of long-term treatment of malignant hypertension. Circulation **18** (pt. 1): 644-651, Oct. 1958.

EFFLER, D. B.: Hiatal hernia. GP **18**: 79-83, Oct. 1958.

EFFLER, D. B.: Surgical treatment of mitral insufficiency; open approach with elective cardiac arrest. Am. J. Cardiol. **2**: 276-280, Sept. 1958.

ENGEL, W. J.: Hypertension of urologic importance. West. J. Surg. **66**: 210-214, July-Aug. 1958.

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ERNSTENE, A. C.: Pre- and postoperative management of the patient with heart disease. Mod. Concepts Cardiovas. Dis. **27**: 479-481, Sept. 1958.

FEIL, H.,* and McCUBBIN, J. W.: Carl J. Wiggers, M.D.; a biographical sketch. Circulation Res. **6**: 548-553, Sept. 1958.

GRIFONE, J. W.,† and BROWN, C. H.: Results of medical treatment of duodenal ulcer complicated by obstruction. GP **18**: 78-85, Sept. 1958.

HALE, D. E.: *In* Cyclopedia of Medicine, Surgery and Specialties in 1958. Philadelphia: F. A. Davis & Co., 1958, Vol. 1: Spinal Anesthesia, 565-581; Inhalation Anesthetic Agents, 477-488; Preanesthetic Medication, 465-470.

HOERR, S. O.; MARTINEZ, W. V.,‡ and ZAVALETA, A. A.†: A Geriatrics Special Exhibit. Cholecystitis. Geratrics **13**: 673-677, Oct. 1958.

HOERR, S. O. (Chairman): Elective operations performed for duodenal ulcer, with their mortality; results of a survey in selected Ohio hospitals by the Survey Committee, Ohio Chapter, American College of Surgeons. Am. J. Surg. **96**: 365-368, Sept. 1958.

HUMPHRIES, A. W.; deWOLFE, V. G., and LeFEVRE, F. A.: Reversibility of pregangrene in the severely ischaemic limb. J. Bone & Joint Surg. **40-A**: 983-993, Oct. 1958.

KATZ, L. N.§; BURCH, G. E.‖; DORFMAN, A.¶; ERNSTENE, A. C.; HECHT, H. H.#, and PARKER, R. L.(: Clinical Progress. Symposium; Unsettled clinical questions in the management of cardiovascular disease. Circulation **18**: 430-446, Sept. 1958.

KRIEGER, J. S., and McCORMACK, L. J.: The indications for conservative therapy for intraepitehlial carcinoma of the uterine cervix. Am. J. Obst. & Gynec. **76**: 312-319; discussion, 319-320, Aug 1958.

LEWIS, LENA, A.; PAGE, I. H., and KOLFF, W. J.: Serum lipoprotein and cholesterol changes in nephrectomized dogs maintained by peritoneal dialysis. Am. J. Physiol. **195**: 161-165, Oct. 1958.

MASSON, G. M. C.; McCORMACK, L. J.; DUSTAN, HARRIET P., and CORCORAN, A. C.: Hypertensive vascular disease as a consequence of increased arterial pressure; quantitative study in rats with hydralazine-treated renal hypertension. Am. J. Path. **34**: 817-834, Sept.-Oct. 1958.

McISAAC, W. M., and PAGE, I. H.: New metabolites of serotonin in carcinoid urine. Science **128**: 537, Sept. 5, 1958.

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NETHERTON, E. W.: A unique case of trichorrhexis nodosa—"bamboo hairs." A.M.A. Arch. Dermat. **78**: 483-487, Oct. 1958.

O'BRIEN, F. W., JR.: Editorial. Radiotherapy at the community hospital level. Radiology **70**: 749-750, May 1958.

PAGE, I. H.; CORCORAN, A. C., and DUSTAN, HARRIET P.: Hypertensive encephalopathy. Heart Bull. **7**: 76-78, July-Aug. 1958.

PAGE, I. H., and McCUBBIN, J. W.: Effect of pentobarbital and atropine on arterial pressure response to ganglion blocking agents. Am. J. Physiol. **194**: 597-600, Sept. 1958.

PAGE, I. H.: Treatment of disorders of cholesterol metabolism. *In* Cholesterol; Chemistry, Biochemistry, and Pathology, edited by R. P. Cook, New York: Academic Press Inc., 1958, pp. 427-433.

SCANU, A.; LEWIS, LENA A., and PAGE, I. H.: Studies on the antigenicity of β-and α_1-lipoproteins of human serum. J. Exper. Med. **108**: 185-196, Aug. 1, 1958.

SKILLERN, P. G.: Menstrual problems in the adolescent. Postgrad. Med. **24**: 163-165, Aug. 1958.

SONES, F. M., JR.: Section on Cardiovascular Diseases. Results of open heart surgery with elective cardiac arrest by potassium citrate in patients with congenital and acquired heart disease. Dis. Chest **34**: 299-316, Sept. 1958.

TURNBULL, R. B., JR.: Intestinal Stomas. Surg. Clin. North America: 1361-1372, Oct. 1958.

TURNBULL, R. B., JR.: Tumors of the Intestine; Method of Rupert B. Turnbull, Jr., M.D. *In* Current Therapy, edited by H. F. Conn. Philadelphia: W. B. Saunders Co., 1958, pp. 293-297.

WASMUTH, C. E.: Standards of care in anesthesiology. Cleveland-Marshall Law Rev. **7**: 403-417, Sept. 1958.

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